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Papers of the Society of Head and Neck Surgeons

Presidential Address

SEVENTH ANNUAL MEETING

In the late nineteenth century, many of the illustrious pioneers of surgery, among them Billroth, Syme, Kocher and Butlin, attempted major excisions of neoplasms of the head and neck area. Discouraging and often catastrophic failures resulting from the inability to establish an adequate airway and failure to control hemorrhage and infection, far outnumbered striking sucesses. Fundamentals of physiology and pathologic anatomy were poorly understood and sound technics of reconstruction had not been perfected to the point where one could point with pride to those patients that survived. Against this background of experience, the advent of radiation therapy offered a hope of effecting a cure with less morbidity and mortality; soon this modality of therapy attracted a majority of patients with head and neck cancer. During this period, however, Crile and Semken in this country and Trotter in England continued an active interest in surgical treatment of these neoplasms. Through their efforts, the necessity of dealing with cervical lymphatic spread became apparent. The principle of block excision of cervical lymphatics was established and technics of effecting these procedures were worked out.

The modern post World War II renewal of interest in surgical management of head and neck cancer was the result of many factors. Problems of anesthesia, infection and nutritional maintenance could now be controlled. A new generation of well trained general surgeons, solidly grounded in physiology, pathology and other ancillary disciplines of surgery, many of whom were returning from military service eager and able to employ surgery in new areas, sensed the limitations and shortcomings of conventional radiation therapy. Playing a major role in this Renaissance of surgery were the careful, detailed studies and records, the stimulus, inspiration and teaching of two men. Both are past Presidents of this Society, Dr. Hayes Martin, former Chief of the Head and Neck Service at Memorial Hospital in New York and the late Dr. Grant E. Ward, who occupied a similar position at Johns Hopkins Hospital in Baltimore.

The management of patients with head and neck neoplasms has, in large part, been a crossroads of many specialties with the radiologist, surgeon, pathologist, reconstructive surgeon, otolaryngologist and chemotherapist all having legitimate interests in the area. Certainly, all groups have made important and substantial contributions to the advances of the field. As a result, any person professing to care for these patients finds it imperative to have a solid knowledge and familiarity with the shortcomings, accomplishments and technics of these varied disciplines. Since the surgery involved is major surgery in every sense of the word, taxing the knowledge, judgment, technical capacity and intrepidity of the responsible surgeon, it seemed likely that those persons with a broad background in general surgery, further fortified by experience, special training and interest in the head and neck area, would

be best endowed to lead and to contribute to the further development of the field.

In the early 1950s, when there was considerable ferment to fragment the American Board of Surgery into a number of subspecialty boards, there was an expressed interest on the part of a number of surgeons primarily interested in the surgery of cancer as well as cancer of the head and neck, to attempt to establish a subspecialty American Board of Cancer. This concept, however, had neither merit nor broad support and was never actively pursued. Nevertheless, there was a real need for an organization of interested people, actively engaged in teaching, research and clinical management of head and neck cancer problems, to serve as a forum for its members, to promote the advancement of knowledge relevant to the area, to stimulate teaching and research and to set standards of competence. In response to these needs and to promote these goals, on November 13, 1954, The Society of Head and Neck Surgeons was organized and the Constitution was adopted at a subsequent meeting on April 14, 1955. From an original organizing nucleus of nine men, the Society has grown to 155 active members, twenty associate members with broad distribution in the United States, Canada and Mexico and with thirty-nine foreign corresponding members from many lands. It is the firm conviction of the Society, that major surgery of the head and neck area is most competently performed by surgical specialists. To promote this objective, the requisites of active membership to this Society are certification by the American Board of Surgery, plus demonstrated competence in the head and neck area by virtue of experience, special training and contribution to the knowledge of the field.

Following the original organizing sessions of the Society, annual scientific meetings have grown progressively in stature, importance and attendance. Reflecting the high caliber of its scientific program, in the past year arrangements have been effected with Dr. Robert Zollinger, Editor, and Mr. Pliny Porter, Publisher of The American Journal of Surgery, to publish annually in this Journal, the papers and scientific proceedings of the Society. To accommodate the large number of papers and to conciliate the often overburdened reader, all papers will be concise and succinct, skeletonized of extraneous material and limited to five pages.

Since we count among our membership most of the eminent teachers, investigators and practitioners of surgery in the head and neck area who will be making reports of their work, the reader should be able to look with confidence to this annual head and neck issue to keep abreast of progress, contributions and controversy of this challenging field of surgery.

ARNOLD J. KREMEN, M.D.
Minneapolis, Minnesota

A Study of Thyroid Cancer in Children

THEODORE WINSHIP, M.D. AND RANDI V. ROSVOLL, M.D., *Washington, D. C.*

From the Department of Pathology, The Washington Hospital Center, Washington, D. C. This study was supported in part by Research Grant CS 9263 from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

IN DEALING with a disease as uncommon as childhood thyroid carcinoma, which in its evolution may span decades, it is incumbent upon investigators to re-evaluate their data periodically. New facts obtained through follow-up of patients and reappraisal of old material are of great value. Combined with the experience of others, they may serve to alter one's concept of a disease. It is with these considerations that we seek to supplement earlier publications.

In 1948 the authors began a study of thyroid carcinoma occurring in children less than fifteen years of age. The world literature was reviewed and subsequently questionnaires were sent to more than 600 hospitals in the United States and Canada to determine the incidence of the disease. Personal surveys were carried out in numerous countries throughout the world, and investigations of the Philippine Islands, Japan and Formosa were conducted for us [*1–5*]. The quest continues and attempts are being made to follow up all the patients in our files. Since our last publication thirty-seven cases have been reported [*6–15*] and three unreported cases have been sent to us. Data have now been obtained concerning 602 patients. Approximately 80 per cent of the patients lived in the United States, the others in thirty foreign countries. This probably does not represent the true geographic distribution of the disease because a more diligent search has been made for patients in this country than elsewhere. The sites of residence of the patients indicate that thyroid carcinoma is unrelated to any specific geographic area.

Many observers have recorded an increasing incidence of thyroid cancer during the past decade. Figure 1 illustrates the occurrence by year of thyroid cancer in children since 1899. The increase begins about 1930 and rises to a rather sharp peak in 1953. The greatest number of new cases appeared between 1949 and 1958. The subsequent decline is becoming less prominent as more cases are recorded.

An attempt was made to elicit a history of previous radiation in only 286 of the patients. Of these, 80 per cent had received therapeutic radiation to the head or neck at some time during infancy or childhood. We feel certain that this figure would be substantially higher if accurate histories could be obtained in all cases. Most of the patients were treated for a

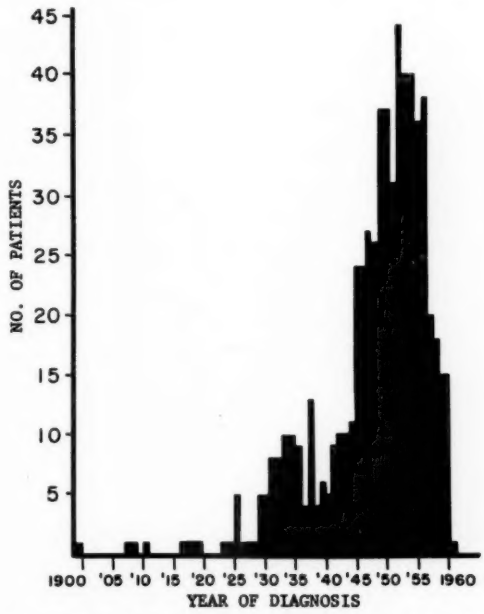

FIG. 1. This illustrates the occurrence by year of thyroid cancer in children since 1899. There was a total of 602 patients.

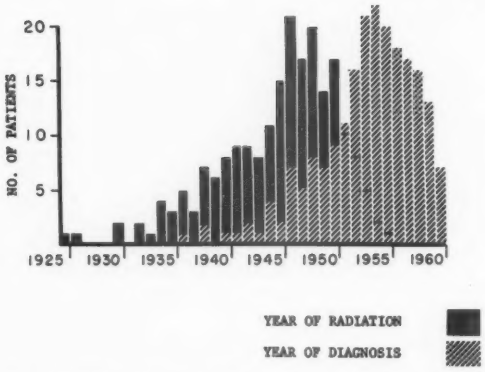

FIG. 2. This shows the date in years that radiation therapy was given plotted against the year of diagnosis for each of 200 patients.

so-called "enlarged thymus gland." Others were treated for hypertrophied tonsils and adenoids, hemangiomas, nevi, acne, eczema and other benign diseases. The dosage administered varied from 180 to 6,000 with an average of 600. Only 12 per cent of the patients receiving radiation lived in Europe and none of them had treatment to the thymus gland. An accurate date of radiation was obtained for only 200. Figure 2 shows this date in years plotted against the year of diagnosis for each patient. The average interval between the radiation and discovery of carcinoma was 8.6 years.

CLINICAL DATA

Thyroid cancer occurred in patients of many different ethnic groups but it was more numerous in Jews and children of Italian extraction than in any other single group. Sixty-two per cent of the children were females. The ages at the time of diagnosis varied from four months to 14.9 years, the average being 9.6 years. Twelve patients were said to have had thyroid tumors at birth which later proved to be carcinoma. In only three instances was there a diagnosis of hyperthyroidism confirmed by laboratory tests.

Adequate clinical details were available concerning 486 of the patients. The chief complaint of nearly all was one or more painless nodules in the neck. The interval between the discovery of the nodule and the establishment of a diagnosis of thyroid cancer varied from two weeks to thirteen years and averaged two years. At the time of initial examination, carcinoma

TABLE 1
INITIAL PHYSICAL FINDINGS IN 486 PATIENTS

Findings	No. of Patients	Per cent
Nodules in neck	363	75
Nodules in thyroid only	116	24
Pulmonary metastases	7	1

was confined to the thyroid gland in only 24 per cent of the children. (Table 1.) The others had either regional or distant metastases or both. In seven patients the first sign of disease was metastatic carcinoma in the lungs. Five of these had been treated for pulmonary tuberculosis before the correct diagnosis of thyroid carcinoma was established. Almost 75 per cent of the patients had cervical node metastases when first examined and in nearly one-third of these the metastatic carcinoma was bilateral. Many of them were in a state of advanced disease when first seen and in twenty instances the patients were described as being moribund, inoperable or nonresectable. It is of interest that three of those described as inoperable lived more than ten years.

THERAPY

Total thyroidectomy and neck dissection were performed on 157 patients and neck dissection was bilateral on twenty. Only about 25 per cent of the neck dissections could be classified as complete. The others consisted of modified procedures referred to as "block" or "modified neck dissections" or simply "node dissection." Forty-one patients were treated by lobectomy and homolateral neck dissection. A total thyroidectomy was performed on fifty-six, a subtotal thyroidectomy on 115 and sixty-seven were treated by lobectomy only. In forty-eight patients radiation was administered following a biopsy. Postoperative radiation in some form was administered to 273 patients. (Table II.) It was prophylactic in some patients and others were treated only if residual tumor was thought to be present. Most of the patients received roentgen therapy but others were treated by teleradium, local radium or telecobalt. The two moribund patients were not treated but all those classified as inoperable or nonresectable received radiation. Seventy-six patients were given thera-

TABLE II
THERAPY FOR 486 PATIENTS

Therapy	No. of Patients	Per cent
Surgery only	165	34
Surgery and radiation	273	56
Biopsy and radiation	48	10

TABLE III
PATHOLOGIC CLASSIFICATION OF 399 CANCERS

Types	Cases	Per cent
Papillary	295	74
Follicular	72	18
Undifferentiated	32	8

peutic amounts of radioactive iodine after surgery and in twenty the pulmonary metastases disappeared. Eighteen of these had papillary carcinoma, and the others had follicular tumors.

Approximately 23 per cent of all patients required more than one operation. Secondary operations were usually performed during the first three years, but five patients required surgery more than twenty years after their original operation. Desiccated thyroid was administered to nearly all the patients from whom a large portion of thyroid tissue had been removed. Many of these have shown progression of their disease and metastases and in only eight instances was regression of tumor reported.

PATHOLOGY

Of the 115 tumors described grossly, 9 per cent measured less than 2 cm, and almost all these were papillary cancers. One was an occult sclerosing carcinoma. The follicular cancers tended to be larger than the papillary variety and the largest tumors were usually undifferentiated in composition. Only seven were described as occurring in nontoxic nodular goiters.

Slides which were taken of 399 patients have been sent to us for histologic evaluation. These are classified in Table III. In the papillary category were placed all the cases which showed any papillation. When multiple sections were prepared, almost all these contained follicles either in the primary or secondary tumor. The follicular cancers were composed solely of malignant follicles without papillary elements but solid foci were often found when multiple sections were cut. Cases without follicles or papillary formations were placed in the undifferentiated group. They were usually solid and composed of a uniform cell type. The undifferentiated cancers were separated into three subgroups. The most common type was composed of sheets of rather uniform small cells. The second subgroup was made up of spindle and giant cells and the third category was designated as medullary carcinoma. Medullary tumors were composed of relatively large cells arranged in compartments lined by strands of fibrous tissue. Not all the tumors in the undifferentiated group were anaplastic and rapidly growing. A few of the patients with small cell carcinoma lived more than ten years and almost half the patients with medullary carcinoma are living after five years.

Gross descriptions of the thyroid glands were not always complete and bilateral involvement of the thyroid lobes was recorded in only eighteen cases. For comparison, in a group of tumors from adults recently examined at the Washington Hospital Center, multicentric foci of carcinoma were found in both lobes in sixteen of eighteen consecutive cases. These were all papillary carcinomas. In the childhood series 76 per cent of the involved cervical lymph nodes contained papillary carcinoma, 15 per cent follicular and 9 per cent undifferentiated. These figures are comparable with the percentage of cell types in the entire group. It appears from these data that the cervical lymph nodes are usually the first site of metastasis regardless of the type of cancer in the thyroid gland. Except for a small increase in the number of undifferentiated tumors no particular cell type was found to be predominant in the patients who had received previous radiation.

FOLLOW-UP

Since this study has shown that patients followed up for only five years are often not free of disease, no effort has been made to evaluate them. Many patients underwent surgery after five years and about 40 per cent of the deaths occurred after the five year period. Two hundred two have been followed up

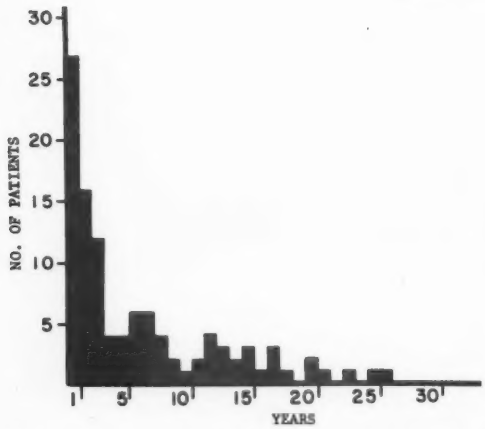

FIG. 3. Follow-up data on 202 patients who have survived over ten years.

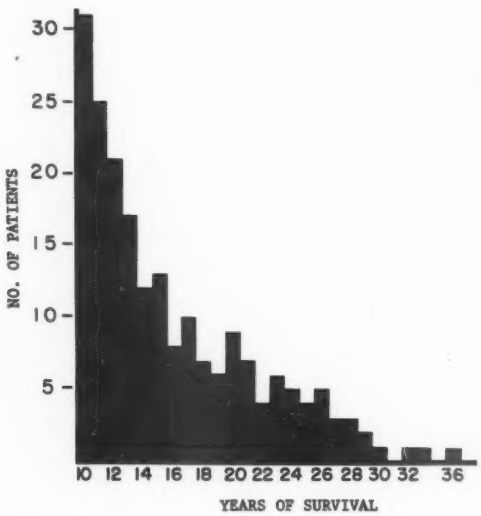

FIG. 4. This shows the number of years from diagnosis to death in 107 patients.

for over ten years. Of these, 159 have been followed up more than ten years, forty over twenty years and three more than thirty years. (Fig. 3.) The treatment for those surviving over ten years was very similar to that of the entire group. Sixty-nine were treated by surgery only, 113 by a combination of surgery and radiation, and in twenty instances the therapy consisted of biopsy and radiation. The types of tumors in this group were found in approximately the same proportion as in the entire series. Many patients with well differentiated cancers had metastatic disease and died soon after initial therapy, while others with undifferentiated cancers have lived for many years despite very little therapy. The exceptions were the two patients with spindle and giant cell carcinoma who died within a year.

Pulmonary metastases occurred at some time in thirty-two patients, and appeared in one patient twenty-two years after her first operations. In one instance, pulmonary metastases have been present for twenty-three years and in another, eighteen years, while eight patients have had pulmonary lesions for more than ten years. In some cases they appeared unchanged while in others there was gradual enlargement. Pulmonary metastases disappeared after the use of radioactive iodine in ten patients in this group. Multiple operative procedures were necessary to control local disease in fifty of the long term survivors. Most of these were reoperated upon only once but multiple procedures were employed with others; one patient has had six operations and still has disease. Sixty-five per cent received therapeutic radiation in some form. In most instances it was administered postoperatively, but in fifteen cases it was the only form of treatment. Assuming that a cure has been achieved for the patients whose lungs cleared after the administration of I^{131}, 15 per cent of those living more than ten years have residual disease. One patient, now forty-eight years old, has had carcinoma for thirty-four years and only recently has become debilitated to any degree. In another patient, massive pulmonary metastases have been present virtually unchanged for eighteen years and she has had no therapy except small doses of radiation to the neck after the removal of a cervical node.

No statistical data have been published to substantiate the suspected hazards of pregnancy on the course of thyroid cancer. In this series twelve women with residual cancer have borne from one to five children and in no instance has an accelerated growth of the tumor been reported during pregnancy or lactation.

MORTALITY

Of the entire group, 107 patients (17.7 per cent died from their disease. (Fig. 4.) More than half the patients who died were in a state

of advanced disease when first seen. Two died without therapy of any sort, twenty-six had been treated by surgery only, thirty-one by surgery and radiation and forty-eight by biopsy and radiation. Eight deaths were classified as postoperative. Sixty-three died within the first five years, nineteen in the second five year period and twenty-five after having had disease ten years or more. Autopsies were performed on twenty-eight patients. Widespread disease was found in only six instances. The others died from carcinoma in the neck or in the lungs or in both areas.

Mustacchi and Cutler [*16*] stated that thyroid cancer progresses five times more rapidly in men than in women, and that survival was poor in men regardless of the histologic variety. In the childhood series the mortality rate for males was only slightly higher than for females. Males comprised 38 per cent of the entire series and 45 per cent of the group who died. It is of interest, however, that 36 per cent of the group living over ten years were males. There was no significant difference between sexes with regard to histologic variety in either those who died or those who lived more than ten years.

COMMENTS AND SUMMARY

Thyroid carcinoma in children is rare. Few physicians have treated a sufficient number of patients to be able to be authoritative. Little is known of its natural history and there is almost no agreement concerning therapy. The chief reason for the disagreement is the paucity of large series of patients with an adequate follow-up, but another factor is the peculiar and unpredictable nature of thyroid cancer. In some instances patients die quickly despite adequate therapy, whereas others with comparable disease, both clinically and histologically, live for extended periods. Thyroid cancer may be dormant for as long as twenty years before regrowth or metastases become evident but in other cases growth may progress as steadily as it does in cancers of other organs.

It is recognized that certain disadvantages are inherent in a study of this type. All the desired information is not available in every case and follow-up data are not always obtainable. Furthermore, it is difficult to evaluate a series of this nature because it covers a long span during which therapeutic methods in surgery, radiology and medicine have changed radically. Nevertheless, a certain amount of useful information has been gained from this study.

Thyroid carcinoma in children has become increasingly prevalent during the past twenty years. No doubt sharper diagnostic acuity has accounted for part of the increase, but a more significant factor is radiation of the thyroid region during infancy and childhood. A history of previous radiation in 80 per cent of the children in this series provides convincing evidence that the use of therapeutic radiation to the neck region of children is a factor in the development of thyroid cancer in some cases. The advisability of the use of diagnostic I^{131} in children is still to be determined.

The histories of the patients show that the first sign of disease is usually persistent, painless, cervical lymph nodes; yet both parents and physicians are slow to recognize the importance of such nodules. Study of the spread of thyroid cancer has demonstrated that metastasis usually occurs first to the cervical lymph nodes regardless of the cell type. There are no histologic criteria upon which to predict the outcome of any given patient. It appears that the prognosis for the patient is more dependent upon the stage of the disease than the cell type or the method of therapy, with the exception of spindle and giant cell carcinoma.

The data on survival do not indicate that one method of treatment has any great advantage over another. It has not yet been proved that total thyroidectomy and radical neck dissection produce better results than various less radical procedures, nor has it been proved that anything has been gained by routine total thyroidectomy rather than lobectomy.

Radiation is said to be of no value in the treatment of thyroid carcinoma; yet 66 per cent of the patients living more than ten years received radiation and fifteen of them were treated solely by this method. Since the pulmonary metastases disappeared after the use of radioactive iodine in twenty patients, it would seem advisable to try this method of therapy on all patients with pulmonary metastases except those with undifferentiated carcinoma.

During recent years beneficial results and decrease in size of metastatic nodules have been reported after continued use of desiccated

thyroid in large doses. Many of the patients in this series have been treated with thyroid compounds over long periods. While encouraging results were reported in eight instances, the other patients have shown either no change or continued growth of tumor and additional metastases.

In the group of long term survivors are twelve women with known residual carcinoma who have borne children. In no instance did pregnancy or lactation activate the tumor. This series is small and additional data are needed before a categorical statement can be made that thyroid carcinoma is independent of hormonal influence.

Much still remains to be accomplished before sufficient knowledge has been accumulated to enable physicians to know the best management of patients with thyroid carcinoma. Until a large number of patients have been followed up for more than twenty years, confusion regarding management will exist. We plan to continue following up the patients in this series until sufficient data have been accumulated to form the basis of sound recommendations for therapy.

Acknowledgment: We are indebted to many physicians and tumor clinic secretaries for contributing information concerning their patients.

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Median Labiomandibular Glossotomy

TROTTER'S MEDIAN (ANTERIOR) TRANSLINGUAL PHARYNGOTOMY

HAYES MARTIN, M.D., H. RANDALL TOLLEFSEN, M.D. AND FRANK P. GEROLD, M.D.,
New York, New York

From the Head and Neck Service, Memorial Hospital, New York, New York.

THE PURPOSE of the present report is to place on record the detailed technic of an ingenious and anatomically sound operative procedure which nevertheless, by reason of its limited usefulness, has hitherto attracted little attention from head and neck surgeons.

From the evolutionary standpoint, the original concept of an operation similar to that described herein was proposed, according to Butlin and Spencer [1], in 1839 by Roux* who split the lower lip and the mandible directly in the midline for a surgical approach to tumors of the anterior portion of the tongue. The procedure was soon thereafter performed by Sédillot [5] in 1844 (varied somewhat by a more oblique incision of the mandible, which, he believed, offered better prospects of reunion) and by Syme [6] in 1857.

In 1929, Trotter [7] reported what he termed a *median (anterior) translingual pharyngotomy*,† in which he extended Roux's midline section of the lip and mandible by splitting the tongue sagitally in the median raphe for exposure of the base of the tongue and midportion of the pharynx. (Fig. 1.) He suggested that the operation would be useful for tumors not only of the base of the tongue but also for those of the midportion of the pharynx (e.g., epiglottis), including its posterior wall. He proposed excision of the median portion of the hyoid bone at the depths of the incision and a horizontal incision across the midportion of the epiglottis and the aryepiglottic folds. Although Trotter gave no case reports, he may have used the procedure in several instances.

Temporary section of the mandible (either median or lateral), with its resuture, has been employed by a number of head and neck surgeons in recent years, e.g., Kremen [2] and one of us (H. M.) [3], in various avenues of approach to the oral cavity and pharynx.

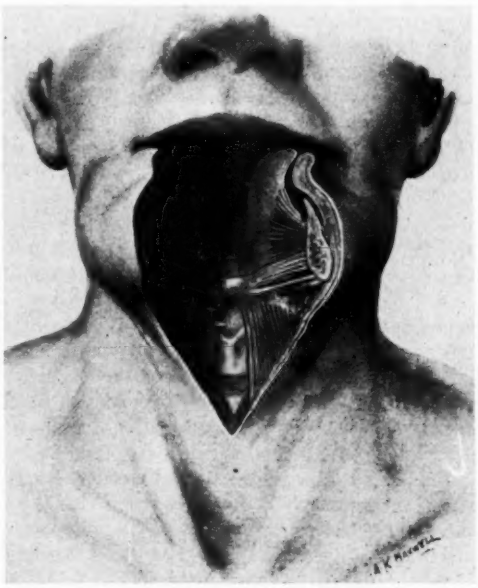

FIG. 1. The only illustration to appear in Trotter's original report. We consider the extent of the incision below the level of the hyoid to be unnecessary.

* Butlin and Spencer [1] give no bibliographic reference for such a published report by Roux and we have been unable to find any such reference even with the aid of the National Library of Medicine, Washington, D. C.

† We find Trotter's terminology somewhat inadequately descriptive of an operative procedure which will be found most often applicable in lingual tumors. We therefore offer the more clearly depictive alternate: *median labiomandibular glossotomy.*

Trotter's operation seems to have received little or no favor, however, until Perzik et al. [4] reported the successful use of this approach in 1958 in an infant two months old with a rapidly growing, already bulky (7 cm.) nonulcerated tumor of the posterior pharyngeal wall, which was causing marked dyspnea and dysphagia. The operation and postoperative course were both uneventful and there were no signs of recurrence one year later at the time of the report. The histologic diagnosis of the surgical specimen was *neurofibrolipomatous hamartoma:* in other words, a benign congenital tumor of mixed cellular origin which, nevertheless, was progressing rapidly toward a fatal outcome. The merits of Trotter's approach in this particular case will be discussed more fully in the concluding paragraphs.

Following Perzik's report, the approach has been used in four instances in the Head and Neck Service at Memorial Hospital, New York City and certain conclusions as to the limitations and advantages of the procedure have been formulated.

ANATOMIC CONSIDERATIONS

In certain portions of the mammalian anatomy the vascular, neural and muscular structures are independently unilateral in character, there being little or no direct vascular or neural communication across the midline. Such is the case in most tissues of the face, oral cavity, pharynx and neck. For this reason, deep and extensive sagittal (midline) surgical incisions can be made directly through these tissues without severing any major blood vessels or nerves. The suture of such incisions usually results in prompt healing with a minimal degree of cosmetic deformity and functional loss. The same anatomic principle applies to some degree in median vertical or horizontal (transhyoid) pharyngotomy and in median laryngofissure. It is obvious that such a principle does not apply when a surgical approach of similar degree is made to the mouth or pharynx from a lateral aspect.

Most of these basic concepts were clearly stated in Trotter's original report. We are of the opinion, however, that some of the advantages and indications claimed by Trotter are of rather doubtful practical significance, as, for instance, his reference to the avoidance of lateral scarring which would interfere with subsequent neck dissection should such a procedure later become necessary. Furthermore, the approach is not quite so satisfactory for hypopharyngeal tumors as Trotter claimed. These points will be discussed further in the present report.

One advantage of Trotter's approach is that it does not endanger the section, the undue stretching of, or any other form of trauma to one or both superior laryngeal nerves, a hazard which always accompanies horizontal pharyngotomy [3], especially if entry is made through the infrahyoid or transhyoid levels. A suprahyoid approach is safer from this standpoint but has the disadvantage that the horizontal length of the opening into the pharynx is shorter than with the transhyoid operation which includes removal of the hyoid bone. Nevertheless, despite any minor variation in the form of horizontal pharyngotomy, there remains the danger of at least overstretching the superior laryngeal nerves and a postoperative failure of their role in the act of swallowing. As is well known, such dysfunction, if it persists, invariably results in aspiration of the ingesta and eventually the fatal complications: aspiration pneumonia and lung abscess. These potential hazards of horizontal pharyngotomy are mong the reasons why Trotter's approach should be given serious consideration in the choice of procedures for surgical access to hypopharyngeal tumors of low grade malignancy.

INDICATIONS AND LIMITATIONS

The usefulness of *median labiomandibular glossotomy* is somewhat limited. Its main practical indications will be found in bulky, noninfiltrating tumors of minor salivary gland origin of the tongue and in histologically benign tumors of the pharynx, having the general characteristics and location as those present in Perzik's case and, also, in some low grade tumors of the extrinsic larynx.

Epidermoid carcinomas of the base of the tongue seldom arise directly in the midline and, moreover, tend to be of a highly malignant anaplastic variety prone to early, often bilateral, metastases. As such, they are almost always better suited to radiation therapy or to a lateral approach combined with neck dissection in one stage [3]. (Case IV here is an exception.) The same is true of epidermoid tumors of the vallecula invading the epiglottis associated with palpable neck metastases. In the absence of palpable metastases, the preferable

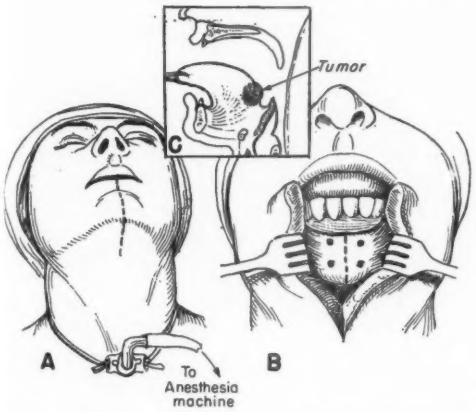

FIG. 2. The incision. After a preliminary tracheostomy and median splitting of the lip (A), holes are drilled through the mandible (B) for fixation of the segments at the time of closure.

surgical approach to epidermoid tumors of the base of the tongue may in some cases be through horizontal transhyoid pharyngotomy [3]. For most tumors of the posterior wall of the pharynx (either benign or malignant) an exposure by Trotter's operation is not greatly superior to the anterior (horizontal) transhyoid approach [3] except possibly in cases similar to that reported by Perzik. A significant example of this limitation is found in Case III here.

In brief, *median labiomandibular glossotomy* will find its greatest usefulness in the less malignant, noninfiltrating tumors directly in the midline of the base of the tongue (Case I, Fig. 12A) and/or valleculae with extension to the anterior surface of the epiglottis (Case IV, Fig. 12B), and in some benign neoplasms of the posterior wall of the pharynx. Any application of the procedure to other situations should be made only after careful consideration of alternate approaches.

CASE REPORTS

CASE I. M. M., a forty-seven year old woman, presented a 2.5 to 3 cm., nonulcerated tumor directly in the midline of the base of the tongue, extending posteriorly about 1.5 cm. short of the vallecula. (Fig. 12A.) There was no evidence of cervical lymph node enlargement. A biopsy report showed "low grade minor salivary gland carcinoma."

She was operated upon (H. M.) on May 25, 1959 and the tumor resected by the technic illustrated

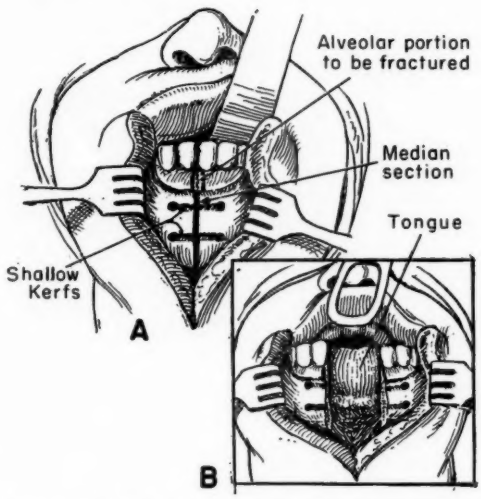

FIG. 3. Section of the mandible. Shallow transverse saw kerfs are made to contain the wire sutures and the mandible is sawed only up to the level of the tooth roots (if any), thereby avoiding possible injury to the roots of the teeth (A). The remaining alveolar portion of the mandible is then separated by fracture (B).

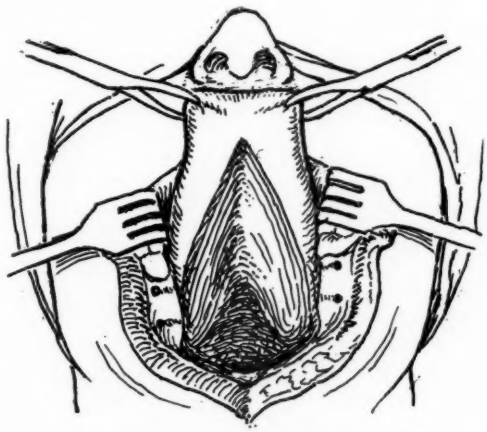

FIG. 4. Splitting the floor of the mouth.

in Figures 2–11. Healing was by prompt primary union of the soft tissues and solid union of the mandible in four weeks. She has remained free of disease for twenty-two months and has no functional defect and no cosmetic blemish except a faint midline scar of the lower lip.

Comment: In this case the procedure had definite advantages over any other approach that might have been used.

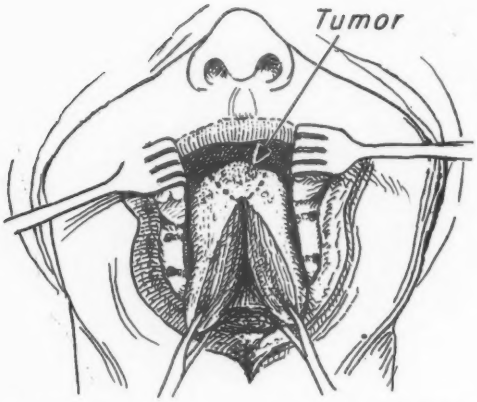

FIG. 5. Splitting the tongue. The incision is carried back short of the tumor.

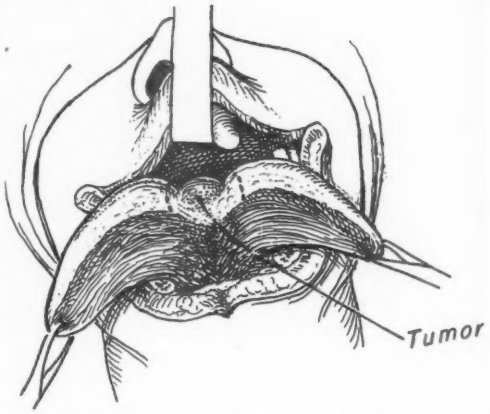

FIG. 6. Outlining the incision to circumscribe the growth. At the lower aspect the incision is carried down to the hyoid which may then be divided and the central portion excised if such an extension is considered useful.

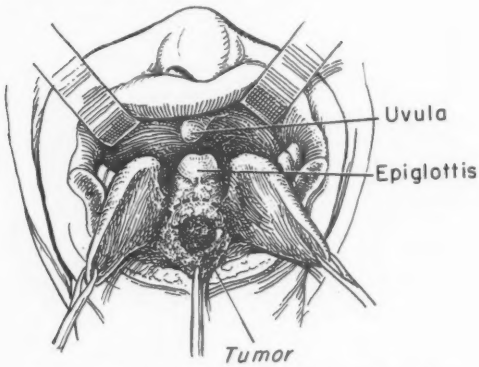

FIG. 7. Delivery of the tumor for its final excision.

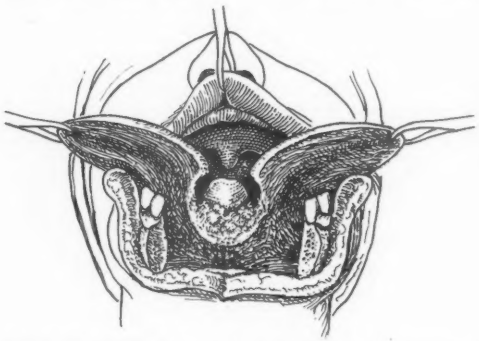

FIG. 8. The surgical wound after excision of a tumor of the base of the tongue.

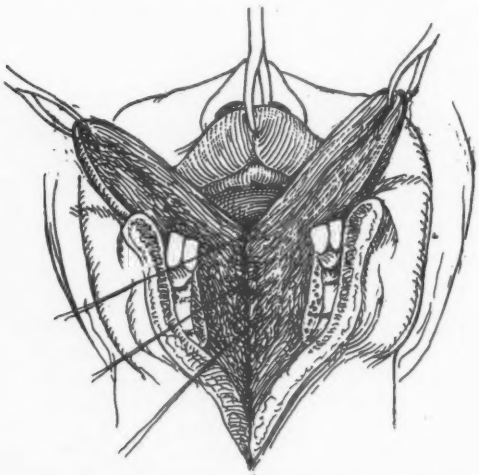

FIG. 9. Layered closure of the wound.

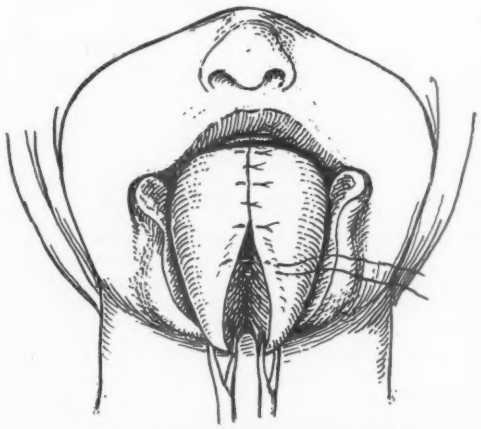

FIG. 10. Layered closure of the wound.

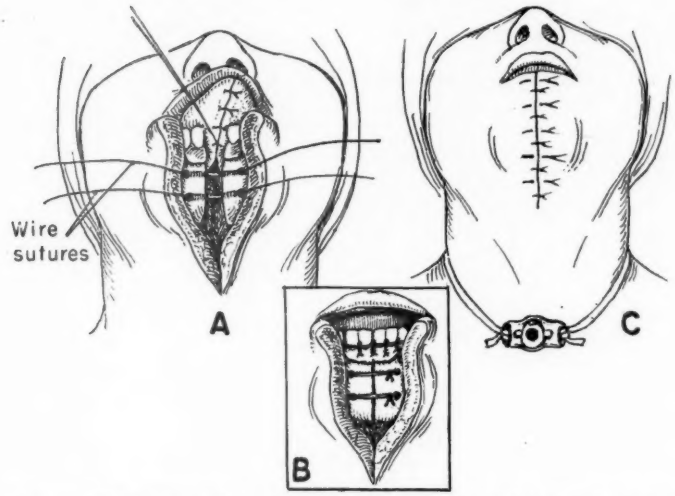

FIG. 11. Final closure of the wound. The wire sutures sink below the surface in the saw kerfs (A) and (B). Dental wiring (B) tends to stabilize further the bony union.

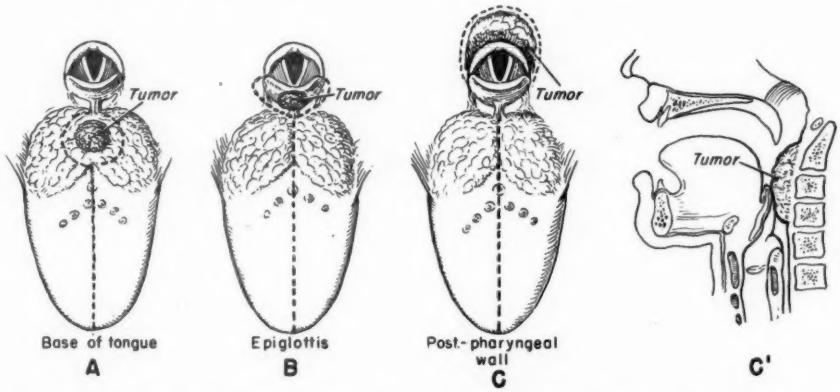

FIG. 12. Anatomic varieties of tumors which can be surgically exposed by median splitting of the tongue. A, centrally located, noninfiltrating tumors of the base of the tongue present the main indications. B, tumors of the vallecula and anterior surface of the epiglottis can be adequately exposed and the epiglottis resected. C, tumors of the posterior pharyngeal wall not extending too far below the level of the arytenoids can be exposed through the tongue-splitting operation, but most are probably better approached through the transhyoid operation.

CASE II. W. G., a seventy year old man, presented a 2 cm. ulcerated lesion almost directly in the midline of the base of the tongue, extending onto the anterior surface of the tip of the epiglottis. (Fig. 12B.) There was a slightly suspicious but rather indefinite enlargement of a right subdigastric node. A biopsy report of the tongue showed "squamous carcinoma, grade 2." He was operated upon (H. R. T.) on June 10, 1959 (Trotter's approach), the primary lesion being widely excised along with the major portion of the epiglottis. Six months later, in January 1960, he was admitted with a definitely enlarged right subdigastric node and a right radical neck dissection was performed. Three months later, another node appeared in the left (opposite) neck and a second radical neck dissection was carried out. The surgical specimens of both neck dissections were reported as showing "metastases to multiple nodes." He was last examined on October 10, 1960 (ten months postoperatively) and was found to be free of disease. He was reported to have died suddenly on Novem-

ber 8, 1960, less than three weeks later, obviously of causes other than recurrent cancer.

Comment: In this case of epidermoid carcinoma with suspicious enlargement of a cervical node, a preferable and more practical approach would undoubtedly have been through the right neck; then, after a neck dissection, the incision could have been extended into the pharynx by horizontal pharyngotomy. The typical clinical course of cervical metastases (bilateral, as in this case) clearly indicates the limitations of the midline approach and the dependence on later neck dissections in such a highly malignant form of tumor. Nevertheless, Trotter's claim that his midline approach does not interfere (by lateral scarring) with subsequent neck dissection was found to be true in this case.

CASE III. M. O., a fifty-three year old white man, was first seen on March 17, 1960 with an ulcerated, granular lesion, measuring 2 by 3.5 cm. on the posterior wall of the pharynx, extending from just above the lower edge of the soft palate down to within about 2 cm. of the arytenoid. (Fig. 12C and C[1].) There was no evidence of cervical lymph node enlargement. A biopsy report showed "squamous carcinoma, grade 2." He was operated upon (H. R. T.), using Trotter's approach, on March 24, 1960, the midportion of the hyoid bone being resected. At the time of the operation it was realized that Trotter's approach for this particular lesion was not superior to that which could have been obtained by a transhyoid horizontal pharyngotomy. The growth was widely excised and the defect was covered by a split thickness skin graft. The graft took in part and healing was complete in four weeks. Six weeks after the operation, an enlarged 2 cm. node was palpated in the left lower neck and on April 26, 1960, a left radical neck dissection was performed. Recovery was without incident but in June 1960, three months after the original operation, a large area of recurrence was found on the right lateral pharyngeal wall. The recurrent growth was considered inoperable from the standpoint of complete resection of the disease and palliative radiation was advised. He returned to his home for this treatment and was reported to have died of his disease on November 26, 1960.

Comment: Trotter's approach did not provide an exposure superior to transhyoid pharyngotomy for this highly malignant growth of the posterior pharyngeal wall except that any risk of injury to the superior laryngeal nerves was obviated. Furthermore, in cases of epidermoid or squamous carcinoma, the chance of early metastasis is so great that a more prudent and practical approach would have been from the lateral or anterior aspect of the neck combined with neck dissection.

CASE IV. V. B., a fifty-eight year old woman, presented a 3 cm. friable papillary type of tumor centered in the right vallecula extending onto the right anterior surface and tip of the epiglottis. Except for its off-center position it resembled the lesion shown in Figure 12B. A biopsy was reported as showing "papillary squamous carcinoma" (i.e., a low grade tumor). The patient was known to be diabetic, under control by insulin.

She was operated upon (F. G.) on February 16, 1961 (Trotter's approach). The hyoid bone was sectioned in the midline to permit more adequate exposure of the extrinsic larynx. The growth was excised with a reasonably wide margin, including a portion of the base of the tongue, the epiglottis and most of the right aryepiglottic fold.

There were no serious postoperative complications. Healing took place by primary union. The tracheostomy tube was removed on the fifteenth postoperative day and she was discharged, able to swallow the contents of a normal diet.

Comment: The anatomic location of this tumor would have made Trotter's approach of doubtful expediency had the growth been of high grade or anaplastic character, especially if associated with palpable metastases or with impending metastases such as are known to occur in a high percentage of cancer of the base of the tongue. In this case, however, the clinical appearance and histologic report indicated that the tumor was noninfiltrating and of low grade malignancy. The immediate successful result would seem to indicate that this surgical approach affords good access to the extrinsic larynx and that portions of the latter structure can be incised through this approach without any difficulty as regards adequate exposure, prompt healing and restoration of function. It is worthy of note that the line of excision in this case did not intrude upon the lingual artery, sacrifice of which might have compromised the arterial supply to that half of the tongue.

MAIN TECHNICAL CONSIDERATIONS

Although the operative technic is given in detail in Figures 2–11, a brief listing of a few of its basic features may be of additional practical significance:

1. Routine preliminary tracheostomy.
2. Preoperative wiring of the teeth (placement of wire loops by the dentist) to facilitate postoperative immobilization of the sectioned mandible.
3. Drill holes and connecting saw kerfs before sectioning the mandible. (Fig. 2 and 3.)
4. Section by motor saw only of the lower aspect of the mandible short of the level of the roots of the central incisors (if present) and deliberate fracture of the remaining portion of the alveolus in the midline. (Fig. 2B.)

POSTOPERATIVE CARE

Nasoesophageal tube feedings and routine measures for oral hygiene such as sprays and irrigations are the same as for any other major oral surgical procedure. The wiring of the teeth may be left for several weeks if the bony union seems at all insecure. The wire sutures of sectioned mandible are well tolerated in most cases.

SUMMARY AND CONCLUSIONS

Median labiomandibular glossotomy (Trotter's approach) is probably uniquely indispensable in certain bulky, histologically benign, pharyngeal tumors similar to those reported by Perzik et al. in 1958 [4]. The procedure clearly has definite advantages in cases of noninfiltrating tumors of minor salivary gland origin (either malignant or benign) arising directly in the midline of the tongue at about the level of the circumvallate papillae (Case I here).

In the average case of epidermoid carcinoma of the base of the tongue, it is our opinion that Trotter's approach is seldom suitable, especially in those cases with already palpable metastases or in those of high grade malignancy which, on the basis of past experience, are likely to metastasize, often bilaterally. This is our considered judgment despite the apparently successful outcome in Case II here, in which the patient survived free of disease for over a year to die of other causes and despite the necessity for staged bilateral neck dissection. Case IV here is an exception for a posteriorly situated cancer of the base of the tongue which was suitable for this approach both because of the near midline location of the tumor and particularly because of the low grade character of the growth.

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Parotidectomy in the Treatment of Chronic Sialadenitis

OLIVER H. BEAHRS, M.D., KENNETH D. DEVINE, M.D. AND LEWIS B. WOOLNER, M.D.,
Rochester, Minnesota

From the Departments of Surgery, Plastic Surgery and Surgical Pathology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

WHEN a chronic inflammatory process exists in a nonessential organ, the organ usually is surgically removed. This is true for the submaxillary salivary gland when it becomes involved by chronic sialadenitis, but this has not always been true when the parotid gland is similarly involved. The obvious explanation of this is the presence of the facial nerve which transgresses the parotid gland. Injury to or transection of this nerve results in a severe cosmetic and functional defect of the face which is of great concern to the patient and is quite obvious to friend and stranger. For many years the anatomy of the parotid gland and facial nerve was not fully understood, and a satisfactory technic for performing parotidectomy with preservation of the nerve had not been worked out. For these reasons benign tumors of the parotid gland were removed by conservative procedures.

In the treatment of chronic or recurrent parotitis, surgical removal of the diseased gland was almost universally avoided, according to Eddey and McKenzie [1]. In 1935 Dorrance [2] cited the danger of dividing the facial nerve, the danger of postoperative formation of fistula, and the price in time and suffering to the patient as militating against surgical removal of the parotid gland as a satisfactory procedure. In 1942 Beck [3] stated: "Excision of the parotid gland is a formidable procedure and is practically never done except for malignant growths." Gerry and Seigman [4] in 1955 wrote " . . . in general, excision of the parotid gland is not surgically feasible in the management of chronic parotid sialadenitis."

If the risk of injury to the facial nerve is sufficient to warrant enucleation of the potentially dangerous mixed tumor rather than parotidectomy, then this reluctance toward the performance of parotidectomy for the benign condition of parotitis is consistent.

Rather than parotidectomy, as previously reported [5], the treatment for chronic or recurrent parotitis has involved the employment of various agents and procedures including radium and x-ray therapy, as mentioned by Adner [6] and Dorrance [2]; dilatation of Stensen's duct by probes and liquids, as in the performance of sialography reported by Hobbs and associates [7] and Pyrah [8]; removal of septic foci, such as teeth and tonsils; use of agents to decrease the viscosity of salivary excretion such as potassium iodide and pilocarpine; massage; oral hygiene; autogenous vaccines; and, more recently, antibiotic therapy. The effectiveness of these conservative approaches to the problem must be viewed in the light of several factors. At the outset it should be recognized that the fact that no single method has been clearly demonstrated to be superior to the others tends to cast some doubt on the effectiveness of all of these approaches.

The protean nature of chronic or recurrent parotitis makes evaluation of a given method of therapy extremely difficult. We are not herein considering other types of inflammation of the parotid gland such as epidemic, postoperative or acute suppurative parotitis. Rather, we are considering the type of inflammation well described by Bigler [9] and Payne [10] in which there are persistent or recurrent periods of swelling and pain in one or both parotid glands. Initially the infection is generally considered to ascend via Stensen's duct. Many believe that the inflammation is secondary to

an inflammation or abnormality about the teeth or elsewhere in the mouth. Often various organisms, most frequently Streptococcus viridans, can be cultured from the duct. Although only a small percentage of calculi of the salivary glands occurs in the ducts of the parotid gland, calculi can be the causative factor of chronic parotitis. Occasionally, a patient has multiple small calculi scattered throughout the parenchyma of the gland. If these patients are experiencing repeated periods of pain and swelling, with low grade fever, they are candidates for parotidectomy. On the other hand, a patient may have a single stone in the duct for which only simple extraction is necessary. As the condition of chronic parotitis progresses, in all probability some obstruction from the inflammatory process is a factor in progression of the disease.

In patients with chronic or recurrent parotitis, untreated or treated conservatively, frequency, duration and severity of the bouts vary greatly. Some patients have a single mild episode, lasting a day or two. Commonly, a patient will have a bout of pain and swelling of the parotid gland that persists for several days or weeks. The symptoms may recur once or twice in the same or opposite gland at intervals of weeks or months, never to return again. Other patients have frequently recurring to constantly severe trouble for years. This can occur whether or not the patient has received any or several of the various treatments ordinarily used. It is in this group of patients that we believe that superficial or total conservative (nerve preserved) parotidectomy is indicated.

In 1958 five patients having chronic parotitis, who had been treated by parotidectomy, were reported [5]. Since the time of this report twenty-four other patients have been treated in a similar manner. Experience with the twenty-nine cases forms the basis of our report. One patient had bilateral parotitis and underwent bilateral parotidectomy, so a total of thirty operations were performed on the twenty-nine patients. The sex ratio was sixteen male to thirteen female patients. The average age was 51.3 years, the youngest patient being four years of age and the oldest eighty-one. The preoperative diagnosis in the four year old girl was tumor; however, she had experienced recurrent swelling and pain in the parotid region. The right parotid gland was involved in fourteen patients, the left in fourteen and both glands were involved in one patient.

The primary symptoms were swelling and pain in the parotid region. In twenty-five cases swelling was reported in front of and below the ear for an average of 5.1 years. In eleven patients the swelling was recurrent, and in all of them the history of the condition was diagnostic of chronic sialadenitis. Eighteen patients had had pain, many of them experiencing repeated episodes of acute pain in the parotid region for many years. Early in the course of the disease the pain was associated with eating, but later this was not necessarily so.

Four patients had passed one or more stones from Stensen's duct. Gross dilation of the main duct was noted in one patient. One patient had evidence of paralysis of the facial nerve. Preoperatively the possibility of a tumor of the parotid gland was considered, although none could be felt; however, the tissue removed by parotidectomy showed chronic sialadenitis. The nerve was observed to be essentially normal. Subsequently, the paralysis was thought to originate in the central nervous system. This patient died of vascular disease two months after operation.

Nineteen patients had received previous treatment for their condition, consisting of heat, massage and antibiotics. In six patients the parotid duct had been probed and in three of these, stones had been extracted or had passed spontaneously. Vaccines had been used in three of nineteen patients without significant improvement. X-ray treatments, used in one patient, were of some help.

X-ray examination was performed in nineteen cases. In seventeen instances dental roentgenograms were taken to show the parotid gland and its duct, or roentgenograms of the skull were taken to show the soft tissue in the region of the parotid gland. In eight cases evidence of stones was seen in the gland or the duct. In an additional two cases, deposits of gravel were seen in the parenchyma of the gland. In two patients sialograms were taken; in one of the two patients a stone was seen and in the other there was narrowing of the main duct with dilatation of the ductal system in the gland and delayed emptying of the ductal system.

In seventeen patients the symptoms and findings were typical of chronic recurrent

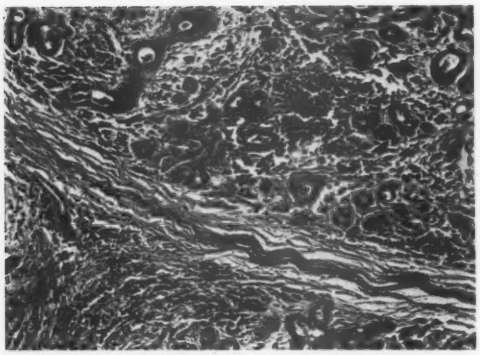

FIG. 1. Chronic sialadenitis. Note loss of acinar tissue and associated chronic inflammatory change. (Hematoxylin and eosin stain; original magnification × 160.)

parotitis and a preoperative diagnosis of this condition was made. In another four patients parotitis was considered but the lesions were thought to be tumors: cysts in two cases, mixed tumor in one and Warthin's tumor in another. On physical examination in eight cases the lesion was considered to be a tumor, even though the history of pain and recurrent swelling of the parotid gland was suggestive of inflammation.

Six of the twenty-eight patients with unilateral involvement underwent total conservative parotidectomy (nerve preserved). In the other twenty-two, subtotal parotidectomy was performed. The portion of the parotid gland superficial to the facial nerve was removed along with the main duct, and the small deep portion of the gland below the nerve was left. In the one case of bilateral involvement, total parotidectomy was performed on the left side and subtotal on the right. The facial nerve was preserved in all instances. There were no hospital deaths. The average hospitalization was 4.3 days. Morbidity was minimal. Drainage from the wound was not a problem except in one patient in whom it persisted for three weeks; in most patients the operative site was healed in a week to ten days. In five cases (17 per cent of twenty-nine operations), not including the one case of preoperative paralysis, slight weakness of the facial muscle followed operation. In all instances function returned to normal within a few weeks.

The first patient was operated on October 25, 1955, and the last patient on December 19, 1960. At the time of this study, all patients are living except the one previously mentioned. Until January 1, 1961, only one patient had had any further trouble. This patient had a recurrent attack of pain and swelling on the operated side four months after operation. He had undergone subtotal parotidectomy and undoubtedly the deep part of the gland was the focus of recurrence. All other patients have had excellent results. No permanent damage to the facial nerve has occurred. Frey's syndrome (gustatory sweating) has developed in only a few patients and in none has it been a significant problem.

PATHOLOGIC FINDINGS

The pathologic findings varied somewhat on microscopic examination of the tissue removed. In two cases there was periductal inflammatory reaction without significant fibrosis, while in one case there was slight chronic inflammation with fat replacement. Cystic dilatation of the ducts with advanced inflammatory response was seen in four cases. Twenty-three specimens showed typical chronic sialadenitis. Microscopically the picture in these was one of chronic inflammation with loss of acinar tissue and varying degrees of compensatory fibrosis. (Fig. 1.) The inflammatory infiltration consists mainly of lymphocytes and plasma cells. In cases associated with obstruction, the ducts show moderate dilatation with occasional squamous metaplasia of lining epithelium. In fourteen specimens calculi were found in the ductal system of the gland.

Criteria for the selection of patients for surgical treatment are not clearcut. Operation is not recommended for all patients with recurrent parotitis, as many or most will have only one or a few mild episodes and no further trouble. The indications must be based on the clinical picture, namely, the distress caused the patient by the disease, frequency of attacks, and duration of the trouble. The decision to operate also must be based somewhat on the experience of the surgeon in performing parotidectomy, with preservation of the facial nerve. In the cases in which parotitis was the preoperative diagnosis, all symptoms were severe enough to warrant surgical intervention. It is interesting to note that in some cases in which the preoperative diagnosis was tumor and in which the history was not suggestive of parotitis, the pathologic findings were identical to those in which the symptoms

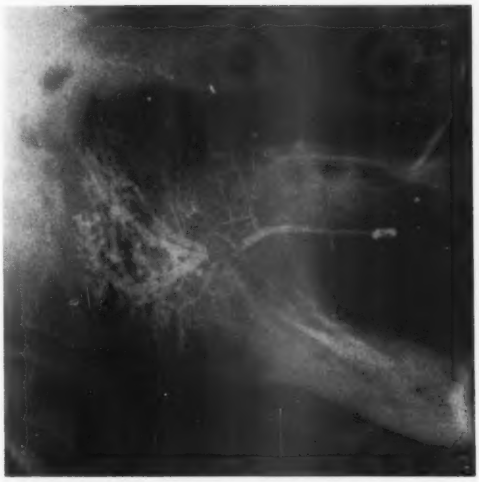

FIG. 2. Sialogram of the left parotid gland in a sixty-six year old man who had recurrent attacks of chronic parotitis for six months. Obstruction of the duct can be seen with dilatation of the ductal system behind the obstructed region. The other ducts are normal.

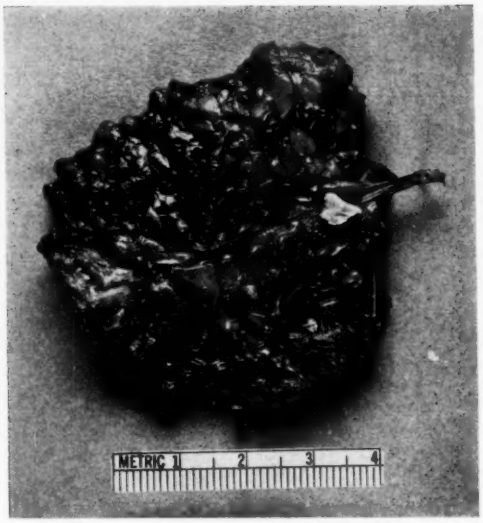

FIG. 3. The surgical specimen removed by subtotal parotidectomy reveals a stone in the duct at the site of the obstruction.

and pathologic findings were typical of chronic parotitis. In some instances stones were present.

In all twenty-nine cases we are convinced that the disease had progressed to the extent that there were irreversible changes in the gland with the resultant element of obstruction, and that hope for spontaneous or medically induced remission did not exist.

Sialography or roentgenographic examination of the parotid gland may present findings that would support the decision to recommend parotidectomy. However, if the nature of the patient's symptoms qualified him for parotidectomy, the absence of confirming signs by sialography or roentgenography would not affect the qualifications. Conversely, if the nature of the patient's symptoms were such that he was not believed to be a candidate for operation (in the absence of a tumor), any roentgenographic evidence of sialadenitis would not make him a candidate. A roentgenogram will reveal evidence of a stone in the gland and a sialogram will demonstrate obstruction of the parotid duct and dilation of the ductal system. (Figs. 2 and 3.)

Some patients present a localized mass in the parotid gland which, clinically, cannot be differentiated from a neoplasm. These patients should be given the benefit of exploration, even though sialography shows changes in the ducts suggestive of sialadenitis. Sialography provides a good outline of the ductal system but, unfortunately, it does not show the parenchyma of the gland.

TREATMENT

Tumor or sialadenitis can be present with or without sialographic evidence of it as shown by Rose [*11*]. Any localized mass in the parotid gland should be treated as a neoplasm until its pathologic nature is known; and any sialadenitis, because of its benign nature, should be treated surgically only on the basis of the clinical picture and not on the basis of ancillary changes in the ductal system found by sialography.

The hazard of injury to the facial nerve should no longer be a deterrent to parotidectomy when this procedure is indicated. If the trunk of the facial nerve is exposed as it enters the substance of the parotid gland, that part of the gland superficial to the nerve can be dissected from the trunk and its branches, with direct visualization and little danger of permanent injury to the nerve [*12*]. There is less danger of injury to the nerve by this method of parotidectomy than there is in enucleating a mixed tumor, for example, because of the direct visualization of the facial

nerve from the start. However, in instances of chronic parotitis, the technical difficulties of exposure of the facial nerve are greater because of the pathologic changes in the gland. Nevertheless, parotidectomy can be accomplished without permanent injury to the nerve. Temporary weakness of the facial muscles may be present for a few days to a few weeks, however. This was true in five cases in this study. In no instance was there permanent injury to the nerve.

Superficial parotidectomy was used in preference to total parotidectomy in twenty-three of thirty glands. This was done since it was believed that the lesser procedure usually produced the desired result and that nothing was to be gained by performing a more extensive procedure. To remove the small remaining portion of the gland which is deep and near the nerve increases the hazard to the facial nerve, but in only one instance was it responsible for recurrent symptoms. This experience, however, will influence us in future cases to excise the deep part of the gland whenever this part comes into question.

SUMMARY

A series of twenty-nine cases is presented in which thirty parotidectomies were performed for recurrent chronic sialadenitis. The results during the follow-up period have been excellent, except in one case in which subtotal parotidectomy had been performed and a recurrence developed five months later. Based on the experience in this series it is recommended that when symptoms of chronic or recurrent parotitis are of sufficient severity and duration and do not respond to conservative measures, subtotal or total conservative parotidectomy should be performed. With proper technic these procedures can be performed without danger of injury to the facial nerve and with complete relief of symptoms.

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Acinic Cell Carcinoma of the Parotid Gland

A CLINICOPATHOLOGIC REVIEW OF ELEVEN CASES

THEODOR B. GRAGE, M.D., PAUL H. LOBER, M.D. AND STUART W. ARHELGER, M.D.,
Minneapolis, Minnesota

From the Department of Surgery and Pathology, University of Minnesota Medical School. This work was supported in part by a grant from the Minnesota Division of the American Cancer Society.

ACINIC cell carcinoma of the parotid gland is a rare neoplasm. Foote and Frazell reported twenty-one cases of this tumor at the Memorial Center for Cancer and Allied Diseases among 766 parotid tumors [*1*]. Beahrs, reviewing 712 parotid tumors treated at the Mayo Clinic, found twenty-four cases of acinic cell carcinoma, an incidence representing 3.4 per cent of all parotid tumors and 16.8 per cent of all primary malignant tumors of the parotid gland [*2*].

A recent review of 272 tumors of the major salivary glands treated at the University of Minnesota Hospitals from 1932 through 1960 disclosed eleven acinic cell carcinomas, comprising 16.9 per cent of all primary malignant tumors of the parotid gland [*3,4*]. It is the purpose of this report to describe the clinical and pathologic features of these eleven cases and to emphasize the potential for malignancy of this neoplasm.

CLINICAL OBSERVATIONS

The tumor occurred in seven women and four men, ranging in age from eighteen to eighty-four years at the time of admission. The age at which the tumor was first noted by the patients ranged from fourteen to sixty-four years, an average age of forty-one years. Four patients were eighteen years old or less at the time the tumor was first detected.

Duration of symptoms varied from three months to twenty years, an average of 5.7 years. Of three patients in whom the tumor had been noted for less than six months, two have subsequently died from the neoplasm and the third has evidence of distant metastases. However, another patient died from extensive local disease seven years after excision of a tumor, which had been present for twenty years prior to surgery.

Symptoms and findings on physical examination were deceptively similar to those found in patients with mixed tumors, which was the usual preoperative diagnosis. The most common complaint was of a slowly growing, nontender, palpable mass. However, two patients experienced considerable facial pain prior to the institution of any therapy. On examination the tumors usually felt firm and were slightly movable. In two patients the tumor appeared fluctuant and in four patients it was moderately tender to palpation. Facial weakness was not noted in any of the patients.

PATHOLOGIC FINDINGS

Grossly the tumors varied in size from 1 to 9 cm. in diameter. A thin but definite capsule could be made out, particularly in the primary tumors, from which connective tissue septa further subdivided the tumor, giving the neoplasm its characteristic lobulated appearance. On cut section the color ranged from grayish white to reddish tan with a glistening surface. The tumors were friable and occasionally cystic.

On microscopic examination the neoplastic tissue appeared to be made up almost entirely of well differentiated, rounded or polygonal epithelial cells with scanty stroma. In a typical tumor the epithelial cells were in close contiguity to each other and frequently arranged into fairly well formed acini. (Fig. 1.) Considerable variation from this pattern occurred. In some areas the epithelial cells formed gland-like

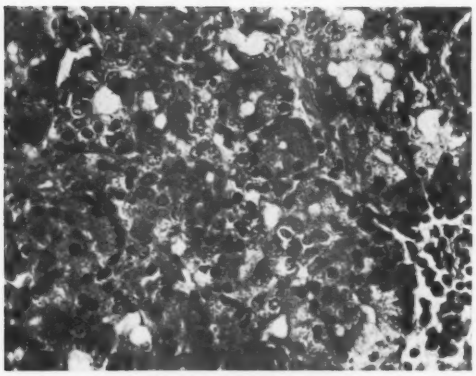

FIG. 1. Arrangement of epithelial cells into poorly formed acini (U. H. 51–3156). Hematoxylin and eosin stain, original magnification × 380.

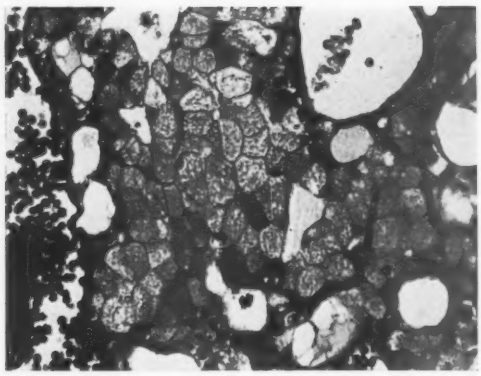

FIG. 2. Abundant granular cytoplasm in large epithelial cells; note resemblance of neoplasm to normal parotid gland (H. O. 38–1812). Hematoxylin and eosin stain, original magnification × 380.

structures and in others a cystic papillary appearance predominated.

The abundant, granular cytoplasm exhibited a strikingly basophilic cast. In two tumors the granularity was so pronounced as to suggest zymogenic granules. (Fig. 2). In other areas the cytoplasm of the epithelial cells was almost water clear.

The nuclei were usually small, dark staining and in an eccentric position. However, in some tumors the nuclei were larger but almost always of uniform size and mitoses were rarely seen. Throughout the tumor tissue numerous intercellular spaces were noted, which frequently coalesced to form larger clear areas.

In four of the primary tumors the neoplasm had invaded the capsule and in several recurrent carcinomas, tumor cells had infiltrated into the surrounding structures. Metastases to regional lymph nodes were observed in two cases. Mucicarmine stains in six of eight tumors that were studied showed stainable material, a finding contrary to some previous reports.

The structural similarity of the neoplastic epithelial cells to the normal acinar cells of the parotid gland, the formation of acini in the tumors and the absence of ductal elements point to the origin of this tumor from the serous cells of the parotid gland. This view is further supported by the cytochemical studies of Azzopardi and Smith, who found a striking correlation between the histochemical characteristics of the epithelial cells of an acinic cell carcinoma and the serous cells of the normal parotid gland [5].

RESULTS OF TREATMENT

Treatment in this group was almost entirely surgical. (Table 1.) Three of the patients, all treated by superficial lobectomy, have been operated upon too recently to permit an evaluation. The remaining eight patients have been treated more than five years ago, with a follow-up period from six to twenty years for the survivors. All patients returned for follow-up examination.

There were recurrences in three of five patients treated for primary tumors and in two of three patients treated for recurrent tumors. Since simple excision had been the initial treatment in seven patients with subsequent recurrence in six of them, the inadequacy of this form of therapy is obvious.

Three of these eight patients died from extensive recurrence and a fourth patient is moribund from locally recurrent tumor and metastases to the cervical spine. Duration of the disease from onset of symptoms to the time of death from the neoplasm averaged thirteen years.

The insidious nature of acinic cell carcinoma is well demonstrated by a fifty-seven year old man (W. M.) who underwent excision of four discrete tumor nodules, which had been present for three years. The primary tumor had been excised thirty years previously and the patient had been free of symptoms for twenty-seven years. In another patient the time interval between excision and recurrence was nine years.

The value of radiation therapy is difficult to assess in this small group. In none of the four

TABLE 1

CLINICAL DATA FOR ELEVEN CASES OF ACINIC CELL CARCINOMA

Patient	Previous Treatment	Treatment at University of Minnesota Hospitals	Recurrence	Treatment of Recurrence	Follow-up Data Since Treatment at University of Minnesota Hospitals
I. T.	No	Excision	Yes	Radiation	12 yr., alive with local disease and metastasis to cervical spine
M.C.	No	Excision	No	...	22 yr., N.E.N.*
M. D.	No	Excision	Several	Radical total parotidectomy, radiation	5 yr., D.O.N.†
M. C.	No	Excision	Yes	Unknown	7 yr., D.O.N.
W. M.	Yes (excision)	Excision	Yes	Radical total parotidectomy, radiation	10 yr., since last surgery, N.E.N.
M. M.	Several excisions	Radical total parotidectomy	Yes	Radiation, radon	3 yr., D.O.N.
I. B.	Yes (excision)	Superficial lobectomy	No	...	6 yr., N.E.N.
S. D.	No	Superficial lobectomy	No	...	11 yr., N.E.N.
J. M.	No	Superficial lobectomy	No	...	Less than 1 yr., N.E.N.
J. H.	No	Superficial lobectomy	No	...	3 yr., N.E.N.
A. O.	No	Superficial lobectomy	No	...	Less than 1 yr., N.E.N.

* N.E.N., no evidence of neoplasm.
† D.O.N., died of neoplasm.

patients treated for recurrent tumors with radiotherapy was it possible to control the local disease. One might not expect a tumor as well differentiated as the acinic cell carcinoma to be radiosensitive.

Complete facial paralysis following surgery occurred in four patients. In three of them the facial nerve was intentionally sacrificed during the course of a total radical parotidectomy for recurrent invading carcinoma, which necessitated partial resection of the surrounding neck muscles in two patients and partial excision of the zygomatic arch and temporal bone in the third patient.

COMMENTS

Only in recent years has acinic cell carcinoma of the parotid gland been identified as a separate and distinct type of neoplasm. The early literature dealing chiefly with isolated case reports has been well reviewed by Godwin et al. [6]. In almost every instance the tumor, because of its benign histologic appearance, had been classified as an adenoma.

With the first group study by Foote and Frazell in 1953, it became apparent that this tumor was a malignant neoplasm [5]. In sixteen of twenty-one cases, the tumor was recurrent when first seen or recurred following treatment at the Memorial Hospital. Three of the twenty-one patients died from the tumor. Beahrs reported a 55.6 per cent recurrence rate within five years in patients treated at the Mayo Clinic for acinic cell carcinoma [2].

From these figures and from the results of treatment in the patients reported in this paper, it is apparent that surgical treatment in the past has been inadequate for the majority of the patients treated. The potential for malignancy of this neoplasm has simply been underestimated. Yet this tumor, because of its superficial location, lends itself to early diagnosis and is characterized by slow growth and a tendency to metastasize later, and thus should be susceptible to surgical eradication in almost every case.

To reduce the high recurrence rate and improve the results of long-term follow-up study, a more aggressive approach to acinic cell carcinomas is needed. These tumors warrant an operation designed to remove the neoplasm with a wide margin of healthy tissue in all planes. In an occasional case this may be achieved by superficial lobectomy or total parotidectomy with preservation of the facial nerve, depending upon the anatomic orientation of the tumor to the gland and the nerve. In most instances, however, total parotidec-

tomy with sacrifice of all or part of the facial nerve is required for adequate removal of these neoplasms. In view of the gratifying results following repair of the facial nerve by nerve grafts, compromising the patient's chance for cure by doing a less radical operation seems unjustified [7,8,9].

Although metastasis to the regional lymph nodes is infrequent, the indications for a radical neck dissection should be liberal. A frozen section of lymph nodes in the immediate vicinity of the parotid gland may disclose spread not evident otherwise. The use of a radical dissection of the neck in all patients with acinic cell carcinoma is probably not warranted.

SUMMARY

The clinical and pathologic features of eleven cases of acinic cell carcinoma treated at the University of Minnesota Hospitals have been reviewed.

Of seven primary neoplasms treated by simple excision, either at the University of Minnesota Hospitals or elsewhere, six recurred subsequently. Only four of eight patients operated upon more than five years ago are alive and without evidence of tumor.

To reduce the high recurrence rate and to improve the rate of ultimate cure more aggressive surgical treatment of acinic cell carcinomas is urged.

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Parotidectomy for Inflammatory Lesions

SAMUEL L. PERZIK, M.D., *Beverly Hills, California*

From the Department of Surgery, Cedars of Lebanon Hospital, Los Angeles, California.

PAROTIDECTOMY is a formidable procedure only because of the presence of the facial nerve in the field of operation. When performed for neoplasms, some sacrifice of all or part of the nerve is acceptable, if by such omission, fatal recurrence of the tumor might follow. When dealing with inflammatory lesions injury to the nerve must be avoided. As a result the number of such patients who have undergone total or subtotal parotidectomy has been relatively few. Because of this potential hazard and negative viewpoint, many of these patients suffer unnecessarily long periods of continuous or recurring pain, deformity and functional as well as cosmetic alterations which involve time and economic loss.

LESIONS

The groups of lesions to be considered are infections of the parotid gland associated with intraglandular abscess usually postoperatively [*1,2*]; intraglandular inflammatory lymphadenitis; infected parotid fistulas due to salivary duct leakage, foreign body granuloma, first branchiogenic remnants, preauricular sinuses or intraglandular epithelial cysts; sialadenitis and sialangiitis secondary to duct obstruction by calculi, cellular debris, stenosis or infiltrating lesions such as Mikulicz's disease, Boeck's sarcoid and Godwin's benign lymphoepithelioma [*3–5*]; and sialangiectasis (sialectasis, sialodochiectasis), either primary or secondary to any of the factors producing duct obstruction. (Table 1.)

Sialangiectasis, a process resembling bronchiectasis, is a frequent underlying etiologic factor in the presenting clinical inflammatory picture. Although it is often found in the late stage of many inflammatory lesions of the parotid gland, it may be considered a primary disease in a specific group of cases wherein it is generalized and frequently bilateral. In the latter instance it is long standing with recurring periods of usually unilateral, but often bilateral or alternating, swelling of the parotid gland associated with an acute local and general febrile course. Children suffer more frequently from this specific entity. It is presumed that the basic cause is probably a congenital ectasia of the ductal system resulting in recurring duct blockage due to secondary infection of the static secretions.

All of the preceding lesions may be present singly or in various and multiple combinations,

TABLE 1
THIRTY-EIGHT PAROTID INFLAMMATORY LESIONS*

Lesion	No.
Intraglandular abscess	5
Acute or chronic	
Pyogenic, tuberculosis, anthrax, actinomycosis	
Intraglandular lymphadenitis	10
Nonspecific, inflammatory	
Specific (tuberculosis)	
Fistulas due to	7
Salivary duct leakage	
Foreign body granuloma	
First branchiogenic remnant	
Infected preauricular sinus	
Infected intra-glandular epithelial cyst	
Sialadenitis and sialangiitis	7
Due to duct blockage by	
Calculus	
Intraductal debris	
Duct stenosis	
Associated with	
Mikulicz's disease	
Boeck's sarcoid	
Godwin's lympho-epithelioma	
Sialangiectasis	9
Primary, congenital and often bilateral	
Secondary, due to chronic intermittent duct blockage	

* These lesions are never discrete but are usually found in various and multiple combinations.

FIG. 1. Sialangiectasis at an early stage, with clinically recurring parotitis controlled by nonsurgical regimen.

FIG. 2. Sialangiectasis with marked dilatation of the duct in advanced stage cured by total parotidectomy and duct excision with preservation of the facial nerve.

as they are frequently related and associated in the same pathologic process. Duct blockage is a complicating factor in practically all of these processes and may be partial or complete and intermittent or continuous.

PATHOLOGY

The pathologic changes in chronic parotitis associated with fistulas, sialadenitis, sialangiitis and sialangiectasis are similar since they are due to secondary duct and glandular alterations. The main variation is one of degree.

Grossly the pathologic findings are represented by an elastic to firm homogeneous enlargement of the parotid gland. Its enveloping fascia is gray, thickened and edematous and overlaps the anterior margin of the sternocleidomastoid muscle. It often surrounds the embedded posterior belly of the digastric muscle. The main (Stensen's) duct and usually the tributaries of the first and second echelons are often visibly dilated. The ducts and adjacent smaller cystic pockets contain a stagnant cloudy gray-white serous fluid. Frequently a localized nodule, usually preauricular, is persistently present, varying only in size during acute exacerbations. This is due to a trapped serous content in a blocked-off dilated segment of indurated duct. Minute calculi may be scattered throughout the parenchyma. The deep lobe is relatively larger in its relation to the superficial lobe. The facial nerve is more adherent to the surrounding glandular and masseteric fascia and shows less sheen than normal.

Microscopically, lymphocytes, plasma cells and leukocytes are conspicuously present in the interspaces between the atrophic acinar structures. The ducts are dilated and filled with this cellular debris in the midst of a periductal lymphocytic infiltration. Frequent lymphocytic masses with germinal centers alternate with areas of interlobular fibrosis. At times, miliary abscesses are present.

DIAGNOSIS

Because of the tendency to delay institution of definitive surgical therapy in the management of parotid inflammatory lesions, a thorough analysis of the clinical picture is often similarly neglected. If it is believed that the lesion does not represent a neoplasm, various empirical therapeutic measures such as x-ray therapy, compresses, antibiotics or probing and dilatation of Stensen's duct are immediately applied without determining the etiologic basis for the presenting clinical picture, often resulting in harmful prolongation of the disease. Certain routine diagnostic procedures should therefore be instituted immediately. A thorough history may tell whether one is dealing with an acute primary infectious process or a secondary acute flare-up of a pre-existing chronic intraglandular inflammatory lesion.

Careful roentgenographic study of the involved region may reveal the presence of calculi. Roentgenograms which are negative for abnormalities do not rule out occult or nonopaque calculi. Sialangiograms [*6*] will frequently reveal duct blockage or intraglandular disease as differentiated from a periglandular or extraparotid lesion. Marked dilatation of the duct and blunting of the terminal ducts

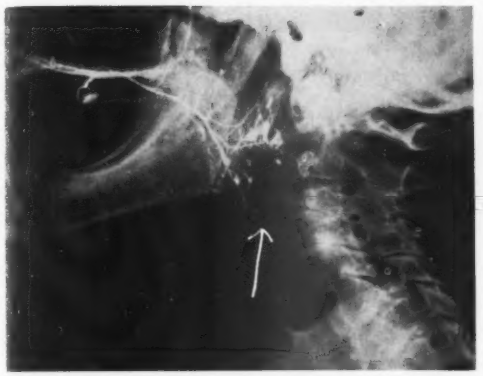

FIG. 3. Simultaneous presence of sialangiectasis and a space-occupying lesion (Warthin's tumor) in the lower pole (arrow) treated by total parotidectomy.

with sac-like formation may indicate specifically the presence of sialangiectasis. (Figs. 1, 2, 3 and 4.) Duct fragmentation is frequently associated with chronic sialangiitis. Such contrast media may even localize the disease to a specific region within the parotid gland such as the deep lobe, superficial lobe or the pterygoid extension of the superficial lobe.

In diffuse involvement, needle exploration and aspiration with histologic and bacteriologic examination of the material obtained may shed further light on the underlying diseased condition. In addition to the more common pyogenic organisms, it is important to consider the possibility of tuberculosis, anthrax and actinomycosis. Close inspection of the mouth of Stensen's duct for edema, redness, purulent discharge or blockage as well as intraoral bidigital palpation should be practiced. This can often best be performed with the aid of a good light, wide retraction of the cheek and tongue in opposite directions and the use of an air spray to dry the region around the duct orifice. The assistance that can be obtained from a complete history, physical examination and the indicated routine laboratory studies such as in suspected endemic parotitis, tuberculosis and infectious mononucleosis is obvious.

The differential diagnosis is primarily to rule out the existence of a neoplasm. In the face of a febrile course this is no problem. In its absence and especially in the presence of a diffuse lesion of recent origin, one must consider in addition to a dormant or chronic inflammatory lesion, the possible presence of an infiltrating adenocarcinoma, a malignant lymphoma, so-called Mikulicz's disease or Boeck's sarcoid. In such infiltrating lesions, a needle biopsy will sometimes be a determining diagnostic factor.

FIG. 4. Focal secondary sialangiectasis with absence of duct markings in much of the gland due to obliterative sialadenitis and sialangiitis. Subtotal parotidectomy with preservation of the atrophic and fibrotic deep lobe permitted safe dissection of the facial nerve with cure of the recurring parotitis.

INDICATIONS AND TECHNIC

Nonsurgical. Once the diagnosis of an inflammatory lesion has been established and a neoplasm ruled out, the basic principles in the management of inflammatory lesions should be instituted. If the inflammation is acute and diffuse, supportive care with specific chemotherapeutic and antibiotic therapy and a minimum of surgery is indicated. Probing or dilatation of an inflammed Stensen's duct or massage of the infected parotid gland can only lead to further injury with possible prolongation of the disability. (Table II.)

Incision and Drainage. When an acute pyogenic parotitis does not respond to supportive measures, the problem of surgical intervention arises. Our personal experience with abortive radiation therapy has not been convincing. If the febrile picture remains

TABLE II
TYPE OF LESION VERSUS SURGERY

Lesion	Type of Surgery	No. of Cases
Abscess	Incision and drainage	5
Lymphadenitis	Subtotal parotidectomy	10
Fistulas	Subtotal parotidectomy	7
Sialadenitis and sialangiitis	Subtotal parotidectomy	2
	Total parotidectomy	5
Sialangiectasis	Total parotidectomy	9

unchanged despite the use of antibiotics and other indicated supportive measures, incision and drainage are instituted. The moment for such surgery is not determined by the presence or absence of fluctuation or by the length of time the disease has existed, but rather by the local picture of increasing spread of the edematous induration and the progressive general phenomena of fever and toxicity. Definite rules for specific timing for surgical intervention cannot be laid down. One should always individualize, leaning toward early, but not too early, surgery rather than too late. The technic for incision and drainage in this situation can, on the other hand, be quite specific. The existing occult or potential pockets of pus are usually found in the region of the external auditory canal, deep to the superficial parotid lobe and deep to and posterior to the lower pole of this lobe. The first layer of the deep fascia, the so-called enveloping layer, surrounds the parotid and forms a junction with the enveloping fascia of the external auditory canal, the masseter muscle and the sternocleidomastoid muscle. Bearing these anatomic points in mind, an approach is made through a preauricular skin incision curved forward below the angle of the mandible. (Fig. 5A.) The fascial junctions referred to are opened by separating the parotid gland from the cartilaginous portion of the external auditory canal and from the anterior border of the sternocleidomastoid muscle. (Fig. 5B.) A finger is then insinuated between the canal and the parotid until the base of the styloid process is palpated. By sliding the tip of the finger caudad, it will detect the taut main stem of the facial nerve. With this as a guide, a curved forceps can safely be inserted between the parotid and masseter muscle. Further separation can be performed deep to the lower pole of the parotid through the fascial connection between it and the anterior border of the sternocleidomastoid muscle, and to each side of the posterior belly of the digastric muscle. (Fig. 5C.) This will open all of the main fascial compartments and result in immediate or delayed evacuation of serum and pus. It is seldom necessary to elevate skin flaps or to puncture the parotid gland through its outer lateral surface.

Subtotal Parotidectomy. With intraglandular lymphadenopathy, a subtotal parotidectomy is usually adequate as in most instances the objective is diagnostic.

In the presence of chronic fistulas, subtotal or total parotidectomy is performed depending on the cause. If the fistula is associated with a single foreign body, a subtotal parotidectomy sufficient to remove the entire tract and the causative agent with dissection and preservation of the facial nerve is usually adequate. In fact, attempting to perform total parotidectomy under these conditions will not add anything to the curative result, and may even result in facial nerve complications due to the frequent intimate fibrous adherence of the contiguous deep parotid lobe to the masseteric fascia. The one exception in which total parotidectomy may be indicated is when the fistula is due to an ulcerated proximal Stensen's duct, usually associated with a calculus. In this instance, leaving large portions of uninvolved gland with dilated secondary or tertiary duct radicals *in situ* may result in troublesome postoperative salivary fistulas which may or may not close spontaneously. They usually close. If the fistula is associated with a first branchiogenic remnant, a subtotal parotidectomy with isolation of the facial nerve will insure a wide and safe excision of the entire tract.

Total Parotidectomy. For all other types of chronic and/or recurring parotitis, total parotidectomy is indicated. This includes cases of multiple calculi, scattered chronic abscesses and sialangiectasis, wherein frequent duct blockage or stasis leads to recurring acute exacerbation of the dormant and chronic preexisting infection. In the presence of multiple calculi, one can anticipate the progressive deteriorating picture outlined so that surgery is indicated without delay. To attempt to treat such a patient by multiple incisions for piecemeal removal of the calculi is more

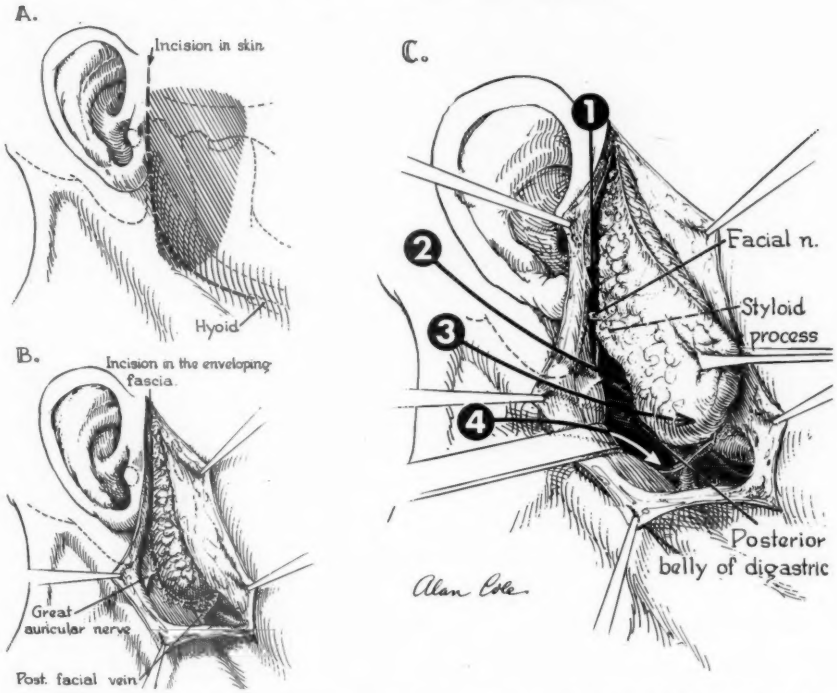

FIG. 5. Incision and drainage in acute parotitis. A, location of "hockey stick" incision with the vertical arm very close to the tragus and the horizontal arm below the angle of the mandible paralleling a natural neck crease and terminating at tip of hyoid bone. B, the incision in the enveloping fascia separates the parotid gland from the cartilaginous portion of the external auditory canal and the sternocleidomastoid muscle permitting direct easy entry into the four main para-parotid spaces. C, arrow (1) reveals the direction of entry into the parotidauricular space using the base of the styloid process as a guide to the main stem of the facial nerve; arrow (2) leads the way into the retromandibular, pterygoid and parapharyngeal spaces by passing between the posterior belly of the digastric muscle and the posterior margin of the mandible; arrow (3) points toward the submaxillary triangle through a pathway between the lower pole of the parotid and the posterior belly of the digastric muscle; and, arrow (4) passing deep to the lower border of the posterior belly of the digastric muscle directs the exploring finger toward the carotid triangle.

hazardous and less definitive than the results obtainable with total parotidectomy. On the other hand, with a diagnosis of sialangiectasis the treatment may be nonsurgical during the first few attacks, as not infrequently the acute infectious flare-ups will cease. However, with persistent or repeated attacks which prove disabling and time-consuming, the attending physician must decide when the law of diminishing returns has been reached and the time for surgery indicated. Total parotidectomy with dissection and preservation of the facial nerve and removal of practically all of Stensen's duct is the procedure of choice in patients with this disease. In the presence of multiple chronic abscesses scattered throughout the parotid, regardless of the cause, total parotidectomy is indicated as soon as the diagnosis is established.

The technic of total parotidectomy has been described elsewhere [7]. Its success is dependent upon an adequate incision and facial nerve visualization. In this series of cases the "Y" incision was used. In most instances the external carotid artery was ligated initially because of the need for maintaining as dry a field as possible for what is usually a tedious and prolonged dissection. The facial nerve is then located at its point of exit from the stylomastoid foramen and traced forward. By this procedure the superficial lobe is first freed and then as the nerve elements are retracted the deep lobe is removed. Dissecting

TABLE III
END RESULTS IN THIRTY-EIGHT CASES

Facial nerve	
Exposed or dissected out	37
Temporary paresis (5 days to 12 mo.)	37
Permanent paralysis	0
Salivary fistulas	0
Auriculotemporal syndrome of Frey	9
Recurrence	0

out the facial nerve is more difficult in the presence of chronic inflammation than of neoplasms, due to the marked nerve-gland adherence present in chronic inflammation. There should be no indication, in surgery for chronic inflammatory lesions, for the deliberate sacrifice of any part of the facial nerve. Closure, drainage and postoperative care are similar to those performed for a neoplasm.

END RESULTS

In this series of thirty-eight patients (Table III) satisfactory results were obtained in all cases. There has been no recurrence of the disabling symptoms which indicated the need for the surgery performed. No permanent injury of the facial nerve occurred. Temporary paresis was present in all cases in which the facial nerve was dissected out, and was of wider extent and persisted longer than that noted in comparable surgery for neoplasms. This undoubtedly was due to the more extensive exposure and trauma to the facial nerve brought about by the marked adherence of the surrounding gland and fascia to the facial nerve. All patients recovered completely from this temporary paresis in a period of five days to twelve months. No permanent salivary fistulas resulted and temporary fistulas were present in two patients for periods of five days to two weeks. The auriculotemporal syndrome of Frey, with preauricular sweating associated with tasty mastication, occurred in nine patients. Cosmetically the results are satisfactory. The scar has become very inconspicuous and except for a minimal, hardly noticeable depression in a few patients, the local topography simulates the untreated side. The result in one patient who underwent bilateral total parotidectomy has been extremely satisfactory from the clinical and cosmetic standpoints and, in addition, there has been no undue intraoral dryness.

CASE HISTORY ANALYSES

Intraparotid Abscess. Of the five patients in this group treated by incision and drainage, intraparotid abscess occurred postoperatively in three and was associated with duct blockage by tumor and sialangiectasis in two. The former three patients were sixty-one, sixty-three and seventy-four years of age and the abscess followed prostatic, gastric and gallbladder surgery. The latter two patients were fifteen and forty years of age. The postoperative patients were treated initially with antibiotics and radiation. The main stem of the facial nerve was identified in all instances.

Lymphadenitis. The characteristic finding in a series of ten patients who underwent subtotal parotidectomies for what proved to be enlarged intraparotid lymph nodes, was the relatively short history of one to three months in six cases, six months in one case and one and a half to five years in three other cases. The location of the lesions was also of interest in that four were preauricular, four of the lower pole and only two were in the pterygoid extension of the parotid gland. There were three male and seven female patients in an age range of eleven to forty-eight years. The histologic report was nonspecific lymphadenitis in seven cases, tuberculous adenitis in one case and granulomatous adenitis, possibly tuberculosis, in two others. The latter three cases were in women in their thirties with short histories of one to six months. The end result in all of these cases has been satisfactory with respect to function of the facial nerve and cosmetic results.

Fistulas. Fistulas involving the parotid area and more specifically the parotid gland have been a deterrent to surgery because of the potential hazard to the facial nerve. As a result, in this group of patients, the disability associated with these lesions has been prolonged far beyond what seemed to be a reasonable period of time due to the utilization of palliative and nondefinitive methods of management. In a series of seven such fistulas, subtotal parotidectomy was performed with dissection and preservation of the main stem and part of the major branches of the facial nerve with excellent results.

There were three cases of preauricular sinuses with abscess formation, all occurring in female subjects, four, seven and thirty-three years of age. The history dated, respectively, from birth, two and four years, with frequent use of surgical drainage, partial excisions, antibiotics and compresses. To insure complete removal of these lesions the facial nerve was identified. The upper division was dissected out and with this in view wide excision of all of the infected, fibrotic and involved areas was then possible. The preauricular bridge of skin was likewise removed to permit better plastic closure by placing the scar vertically as close to the ear as possible.

Three patients with first branchiogenic fistulas arising in a blind cartilaginous reduplication at the medial surface of the external auditory canal and pointing in the infraparotid and submaxillary areas were treated by subtotal parotidectomy with dissection and preservation of the facial nerve. The patients, one female and two male, were nineteen, twenty and thirty-one years of age. The fistulas had been discharging off and on for periods of one to fifteen years, and the patients had been treated by frequent surgical drainage, partial excision, antibiotics, radiation and other symptomatic measures. The associated disability in all instances was both physically and mentally exhausting. By exposing the facial nerve initially it was possible to eliminate safely all the fistulas. In one case, due to marked fibrosis, secondary to prior infection and local surgery, it did not appear to be safe to identify the main stem of the facial nerve as an initial measure. In this instance identification of the main stem was accomplished by picking up the mandibular division first and then tracing it proximally toward the main stem of the facial nerve.

A granulomatous, preauricular fistula secondary to a persistent nondetectable sequestrum of the coronoid process of the mandible was similarly eliminated in a forty year old man after eighteen months of unsuccessful nondefinitive surgical and symptomatic therapy. By tracing out the facial nerve along the fistulous tract, the surgical procedure was continued with greater confidence until the sequestrum was found and removed. Healing promptly followed.

Sialadenitis and Sialangiitis. This group of seven cases occurred in two men and five women in an age range of fifty to seventy-three years. The recurrent attacks covered a period of two to fourteen years. They were associated with duct blockage due to calculi, stenosis and stasis with cellular debris. Despite acceptable anti-inflammatory regimens and radiation, the disease persisted in all instances, with marked local and general disability. All but two patients were treated by total parotidectomy. In the latter two patients (Fig. 4), the deep lobe was so fibrotic and adherent to the facial nerve that it was decided to leave this portion *in situ* to avoid any serious injury to the nerve, especially since it appeared that no active glandular tissue remained. Follow-up study over two to four years without fistulas or recurrence bears out the correctness of this decision. In all instances the facial nerve was dissected out and preserved.

Sialangiectasis. In this series of nine cases, seven were probably primary (congenital) and two secondary to preceding intraductal disease. Both patients with secondary sialangiectasis were elderly (fifty-seven and sixty-one years) and had relatively short histories (two to three months) and concomitant findings of Warthin's tumor (Fig. 3) and Godwin's benign lymphoepithelioma. In the presumably primary group of seven cases, the age incidence was two, five, five, nine, sixteen, twenty-nine and thirty-nine years. There were six male and one female patient. The disease, before definitive surgery, covered periods of three, seven and twelve months, and four, four, six and six years. As time progressed the attacks became more frequent and disabling, occurring as often as every three to six weeks. In all cases antibiotics, radiation, minor surgical procedures and other symptomatic measures were utilized without relief. From one half to four fifths of the life span of three of the children was occupied with a continued symptomatic attack on this disabling disease. By total parotidectomy with dissection and preservation of the facial nerve, the disability was terminated in all of these cases.

CONCLUSION

There are specific indications for surgery in inflammatory lesions of the parotid gland. Vascillation due to lack of judgment or facial nerve phobia may result in serious delay with a concomitant increase in morbidity, compli-

cations and sequelae as well as economic time loss.

The lesions most likely to be associated with such infections are duct blockage due to calculi, stenosis, cell debris and inspissated secretion with recurring sialadenitis or sialangiectasis, and acute and chronic parotitis with abscess formation. Other lesions in this group are the infected cysts and fistulas, vestigial or acquired, and nonspecific and specific intraparotid lymphadenitis.

There are definite indications for incision and drainage, subtotal parotidectomy and total parotidectomy. Relatively, there is a greater demand for total parotidectomy in inflammatory parotid lesions than in tumors. The surgery is more difficult and hazardous due to the perineural adhesions usually present and because there is never an indication, under these circumstances, for sacrifice of any part of the facial nerve.

The satisfactory end results in this group of lesions warrant a greater consideration of surgical intervention at the optimal time.

SUMMARY

The indications and timing for surgical intervention in inflammatory parotid lesions are discussed. The technic of the various surgical procedures are described. Representative case histories are analyzed.

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Auriculotemporal Syndrome (Frey's Syndrome) Following Surgery of Parotid Tumors

H. Mason Morfit, M.D. and David Kramish, M. D., *Denver, Colorado*

From Department of Surgery, University of Colorado School of Medicine, Denver, Colorado.

Following the surgical removal of tumors of the parotid gland one encounters patients who report that when eating, a localized area of flushing and excessive sweating occurs in the general area of the operation in response to the gustatory stimulus. This phenomenon is believed to result from interruption of the auriculotemporal nerve and was described in some detail by Frey in 1925 [1]. Seventy years prior to Frey, a brief report of the same thing was made by Baillarger in 1853 [2] and again in 1897 by Parke-Weber [3].

Essentially all the earlier reports concerned patients who were victims of parotitis associated with a concurrent debilitating disease such as typhoid fever (so common during that period), or in patients who had received a penetrating trauma to the area such as a gunshot wound. The syndrome only occurred in patients with parotitis after incision and drainage had been performed and there are few if any well documented instances in which it appeared in the absence of such therapy.

Since the incidence of typhoid and similar diseases has been considerably reduced, such a clinical setting is now only rarely encountered and the problem is mainly experienced by surgeons engaged in the operative removal of tumors arising from the parotid gland. Therefore, this postoperative syndrome may not be as well known as it could be.

There is of course, no doubt that this syndrome occurs and its existence has attracted considerable attention for years in journals devoted to purely neurologic diseases. Since most surgeons have a hard time keeping up with those journals devoted to purely surgical problems, such articles have escaped their notice and the problem seems to deserve wider circulation before this segment of the medical profession such as has recently been done by Turner, Devine and Judd [4].

The present paper reports the results of an analysis of 100 consecutive patients who underwent removal of the superficial parotid gland with dissection and preservation of the seventh nerve for treatment of a parotid tumor. It does not include patients whose tumor was so small or so located that any lesser operative procedure was performed. This operation is occasionally referred to as "total parotidectomy," although it is generally recognized as a false description since a portion of the gland roughly equivalent to 15 to 20 per cent of the total volume which lies beneath the nerve and for the most part behind the ascending ramus of the mandible is left intact in such a procedure. Nevertheless, this operation has now become accepted as the best way to achieve wide removal of tumor and has supplanted the earlier operations involving attempts to "shell out" the seemingly well encapsulated tumor but which were attended with such a high percentage of local recurrence.

RESULTS OF SURVEY

Incidence. Of the 100 patients, fifty-four reported the syndrome as a direct result of the operation. This is considerably higher than the estimate of 10 per cent made by Martin in a personal communication to Turner, Devine and Judd [4] which is the only other figure we were able to find pertaining to frequency.

Time of Appearance Postoperatively. Of the fifty-four patients reporting this phenomenon,

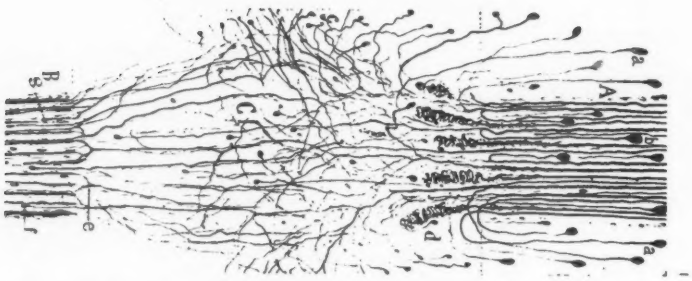

FIG. 1. Peripheral nerve cut at C. From proximal end (A), neurofibrils grow out in fine branches, a few of which may ultimately realign at distal neurilemma sheaths (B). If two nerves lie adjacent, realignment with the "wrong" nerve may occur. (From: Ramon y Cajal, S. [7].)

twenty-five stated that it appeared within three months after the operation, twelve within six months postoperatively, ten within nine months and three within twelve months. Only four patients noted its development after a year or more.

Degree of Nuisance Value. There was a tendency for women to rate the problem as a greater nuisance than men. As a group, twenty-six of the fifty-four rated the nuisance as "mild," thirteen as "moderate," eleven (mostly men) as "not at all troublesome" and four as "very troublesome." The latter four persons (all women) stated they would accept major surgery as a corrective measure; however, since no specific such therapy was seriously offered, it remains questionable as to whether they would actually have followed through.

Degree of Severity with Passage of Time. Since replies to these questions depended mostly on subjective impressions and were made without benefit of any objective measuring scale, considerable variation was reported. However, thirty-three patients reported no change after a year or more, twelve believed it to be worse, six thought it less and only three reported its complete disappearance.

COMMENTS

Reference to other sources is suggested for a detailed study of the mechanism by which this phenomenon is produced. Haxtun [5] has summarized the results of such studies under four possible theories.

1. Parasympathetic secretory fibers to the parotid salivary gland running in the auriculotemporal nerve regenerate along the wrong neurilemma sheath after interruption of the auriculotemporal nerve and come to innervate the sympathetic endings in the skin.

2. Scar tissue in the parotid gland gives rise to excessive tension during parotid activity, causing irritation of sympathetic fibers traversing the gland in the auriculotemporal nerve.

3. The attempts at regeneration of fibers of auriculotemporal nerve strangulated by scar tissue in the parotid gland result in abnormal irritability of the cholinergic nerve endings.

4. The auriculotemporal syndrome is a normally existing reflex deprived of inhibitory fibers by damage to the nerve supply of the area.

The explanation containing the concept of misdirection of regenerating nerve fibers as propounded by Ford and Woodhall [6] seems to fit better than any. The auriculotemporal nerve runs partly in the groove formed by the posterior edge of the ascending mandibular ramus and the cartilage of the external auditory canal. From here it is distributed in fine branches over the preauricular and temporal areas, in part via the terminal branches of the seventh nerve. At this level in its course surgical disruption is produced during operation and surgeons may identify it as a small nerve seldom in excess of 1 mm. in diameter.

At this level the nerve contains: (1) afferent fibers conveying sensory impulses from the skin, (2) vasodilator fibers to the subcutaneous arterioles, (3) secretory fibers to the sweat glands from the cervical sympathetics, (4) salivary secretory fibers to the parotid and (5) vasodilator fibers to the parotid. The salivary secretory and vasodilator fibers to the parotid are parasympathetic and travel via the ninth nerve and otic ganglion to the parotid. An

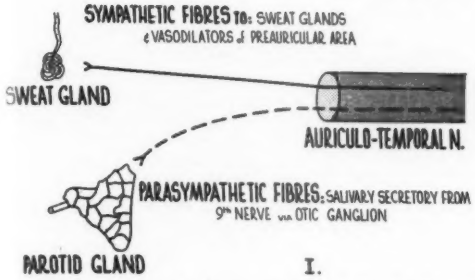

FIG. 2. Diagrammatic representation of distribution of sympathetic fibers to the sweat glands and parasympathetic secretory fibers to the parotid gland as they exist prior to surgery.

injury to the auriculotemporal nerve at the point produced in parotidectomy produces interruption of all five aforementioned pathways.

In the classic studies of Ramon y Cajal [7] what happens when a peripheral nerve is cut has been beautifully demonstrated. (Fig. 1.) There is degeneration of the nerve distal to the cut, the structures ultimately forming sheaths or bands now devoid of all conductive nerve tissue and serving only to mark the former course of the nerve in the tissues. Proximally the degeneration proceeds centrally until the level of the first node of Ranvier is reached. Beginning at this point, attempts to restore the continuity of the severed nerve by regenerative phenomenon are initiated.

Beginning within a few hours after injury, new fibrils begin to grow from this proximal stump forming a brush or tuft, the individual fibrils of which push out in many different directions, some even bending backward and coursing 180 degrees off the original axis of the nerve prior to injury. The degenerating fibers of the distal stump, however, appear to exert a primitive attraction on these new fibers and many will attempt to bridge the point of injury and seek realignment with the degenerating distal neurilemma sheaths. Furthermore, it has also been noted that if two adjacent distal nerves lie close enough together, there may be an intermixture of the regenerative fibrils and the new fibers may enter the wrong nerve.

A schematic representation of the misdirection of regenerating fibers as it applies to the auriculotemporal syndrome is represented in Figures 2 and 3. Once this realignment occurs, the afferent gustatory stimulus travels over undisturbed pathways; however, as the result

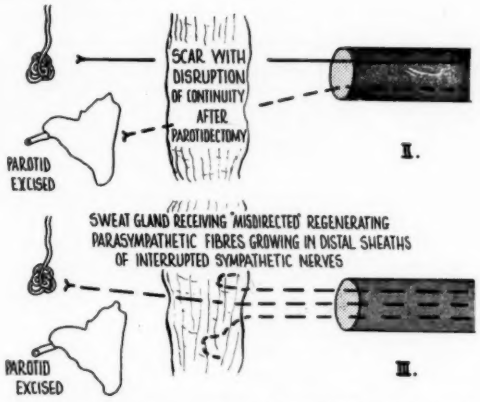
SCAR WITH DISRUPTION OF CONTINUITY AFTER PAROTIDECTOMY
PAROTID EXCISED
II.
SWEAT GLAND RECEIVING 'MISDIRECTED' REGENERATING PARASYMPATHETIC FIBRES GROWING IN DISTAL SHEATHS OF INTERRUPTED SYMPATHETIC NERVES
PAROTID EXCISED
III.

FIG. 3. Auriculotemporal syndrome. When the continuity of the auriculotemporal nerve is interrupted during parotidectomy, the afferent gustatory stimulus travels over undisturbed pathways, but the efferent archs are broken-up by removal of the parotid. The parasympathetic secretory fibers to the parotid may realign by misdirection with the sympathetic nerves feeding the sweat glands.

of realignment, the efferent stimuli can no longer go to the surgically removed salivary gland (parotid) but are misdirected to the sweat glands in the area. The common interval of three to six months postoperatively it takes for the symptom to appear fits well with the time interval required for regeneration of nerve tissue, and its appearance in about 50 per cent of the operative cases would seem well within the range governed by chance as to whether such regenerating fibers ultimately achieve realignment or die in a mass of scar during the abortive attempt.

TREATMENT

Fortunately, most patients will be satisfied with the reassurance that the appearance of the syndrome does not constitute an evil forerunner of any disastrous postoperative complication, that it has nothing to do with whether the surgically removed tumor is going to recur or remain cured, that it occurs with such frequency as to justify acceptance as a common complication of the operation and that it will probably become no worse with the passage of time. The suggestion of some [8] that the syndrome can be abolished by cutting the glossopharyngeal nerve seems hardly worth serious support, particularly since such therapy involves open craniotomy to permit cutting the ninth nerve at the proper level.

Local x-ray therapy directed to the skin area and applied in a dose high enough to destroy the sweat glands has been considered but finds no acceptance in this atomic age by either patient or physician. Turner, Devine and Judd [4] have suggested local application of a cream containing 3 per cent scopalamine hyperbromide as effective. We have had no experience with this remedy, but believe it to be a possibility simple in application and in keeping with the relatively harmless nature of the complaint.

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Statistical Evaluation of 115 Cases of Carcinoma of the Epiglottis (1943 to 1952)

DARIUS K. SHAHROKH, M.D., KENNETH D. DEVINE, M.D. AND EDGAR G. HARRISON, JR., M.D.,
Rochester, Minnesota

From the Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

IN the ten years from 1943 through 1952, approximately 1,400 patients having cancer of the larynx were registered at the Mayo Clinic. Of this group, 116 patients were afflicted with cancer of the epiglottis, which comprised 114 squamous cell carcinomas, one adenocarcinoma and one rare angiosarcoma. The case of angiosarcoma is excluded from this series and will be reported later.

Thus, epiglottic cancer during this period constituted about 8 per cent of all laryngeal cancers diagnosed, a ratio of 1:12. The number of patients seen with epiglottic carcinoma has shown a small but steady increase. During the five year period, 1943 through 1947, forty-nine patients with this condition were registered; from 1947 to 1952, sixty-six were registered and from 1952 to 1957, eighty-one. Of the 116 patients 109 were men and six were women, a ratio of 18:1. The average age of the patients was fifty-seven years, with a range from twenty-four to seventy-seven years. Seventy per cent were in the sixth and seventh decades of life, 8 per cent were more than seventy years of age and 3.5 per cent were less than forty years of age. The youngest patient in the series was a twenty-four year old woman. Review of the family history of eighty-seven patients revealed that 25 per cent of the next of kin had suffered from various types of cancer. Two brothers in our series had identical cancers of the epiglottis. In 3.5 per cent of the cases, multiple primary cancers were located in the air or food passages. It is of interest that 89 per cent of the patients smoked and 63.5 per cent drank alcoholic beverages.

Most patients had been treated prior to admission to the clinic. Twenty-four per cent had had symptoms for more than a year. The most frequent single initial complaint was sore throat. Hoarseness and dysphagia were common complaints and, surprisingly, 23 per cent had hemoptysis. Ten per cent mentioned swollen glands in the neck.

GROSS PATHOLOGIC FINDINGS

Laryngeal Lesions. In sixty-four cases, or 56 per cent of 114 cases of squamous cell carcinoma of the epiglottis, the lesions were either located on the laryngeal aspect of the epiglottis, confined to the epiglottis or extended to adjacent structures including false cords, ventricle, vocal cords and anterior commissure.

Lingual Lesions. In seventeen cases, or 15 per cent of 114 cases, the lesions were either located on the lingual aspect of the epiglottis, confined to the epiglottis or extended to the vallecula and base of the tongue.

Laryngopharyngeal Lesions. In seven cases, or 6 per cent of 114 cases, the lesions were located on the lateral margins of the epiglottis and extended to adjacent structures including the aryepiglottic fold, the pharyngoepiglottic fold, the pyriform sinus and the lateral wall of the pharynx.

Combined Lesions. In twenty-six cases, or 23 per cent of 114 cases, the lesions involved more than one of the aforementioned types. Involvement of the pre-epiglottic space had not been considered as a criterion, because it was difficult to identify the involvement of this region by clinical examination except in advanced cases and also because in 75 per cent of the specimens in which the lesion was confined largely to the epiglottis, the space was involved by cancer.

In 7 per cent of the fifty-six specimens available for study, the cancer involved the free

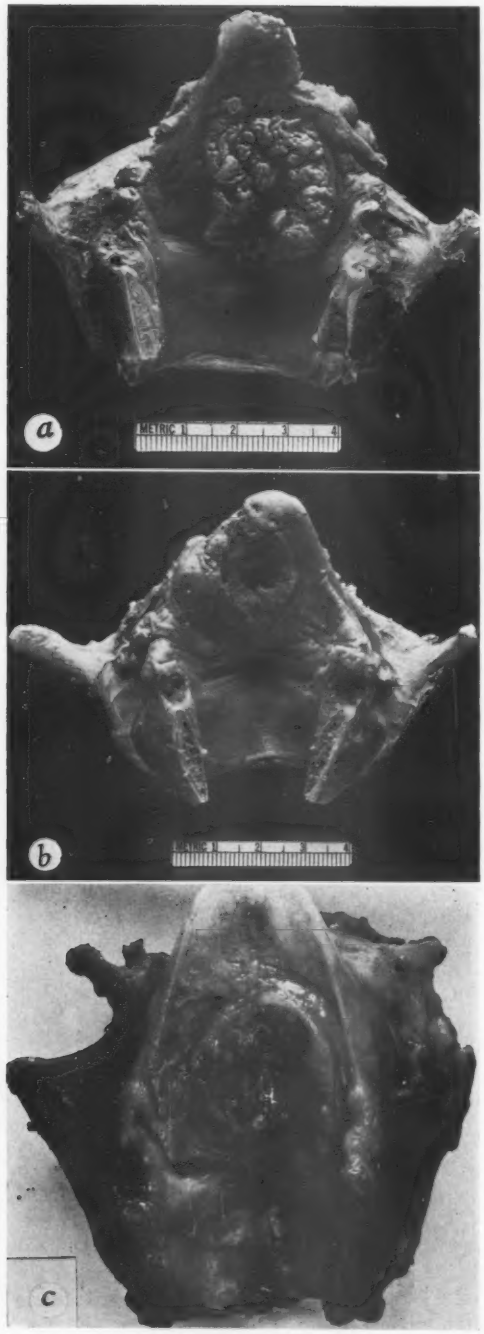

FIG. 1. Variations in gross appearance of squamous carcinomas of the epiglottis. A, fungating, grade 3 squamous cell carcinoma. B, sessile, grade 2 squamous cell carcinoma. C, ulcerative, grade 3 squamous cell carcinoma.

portion only and in 45 per cent it involved the fixed portion or base of the epiglottis. In 48 per cent of the cases the cancers involved both the free and the fixed portion of the laryngeal aspect of the epiglottis. They were lateralized in 16 per cent and involved the complete surface of the laryngeal aspect in 32 per cent.

In the total group of 114 cases of squamous cell carcinoma, 27 per cent of the cancers were confined to the epiglottis without any extension to adjacent surfaces. Seventy-three per cent of the lesions showed evidence of local extension beyond the confines of the epiglottis. In about half of these cases the lesions involved the false cords; in a fourth they involved the valleculae and the base of the tongue, in about a sixth the aryepiglottic fold, and in a tenth the true cords, arytenoids, or lateral wall of the pharynx. In three cases the hyoid bone was involved.

Seventy-five per cent of the cancers appeared as bulky projections or had a cauliflower-like appearance. About 5 per cent were deeply ulcerative and excavating, whereas 20 per cent were flat, slightly elevated, and sessile in appearance. Ulceration was found rather frequently in combination with the other types. (Fig. 1.)

MICROSCOPIC PATHOLOGIC FINDINGS

The epiglottic carcinomas were classified as 114 squamous cell type and one adenocarcinoma. The squamous cell carcinomas were additionally classified as *in situ* and infiltrative.

In Situ Carcinoma. *In situ* carcinoma was found in only one case in which examination of the specimen also showed a grade 1 infiltrative squamous cell carcinoma on the fixed portion of the epiglottis with extension to the false cord on one side. Microscopic examination of a red patch, 1 cm. in diameter on the upper third of the laryngeal aspect of the epiglottis and completely separated from the main lesion, showed a grade 1 *in situ* carcinoma. The silent nature of epiglottic carcinoma *in situ* could account for the rarity of detection of this kind of cancer in this location, whereas cancer *in situ* of the vocal cords is commonly encountered because of early changes in the voice.

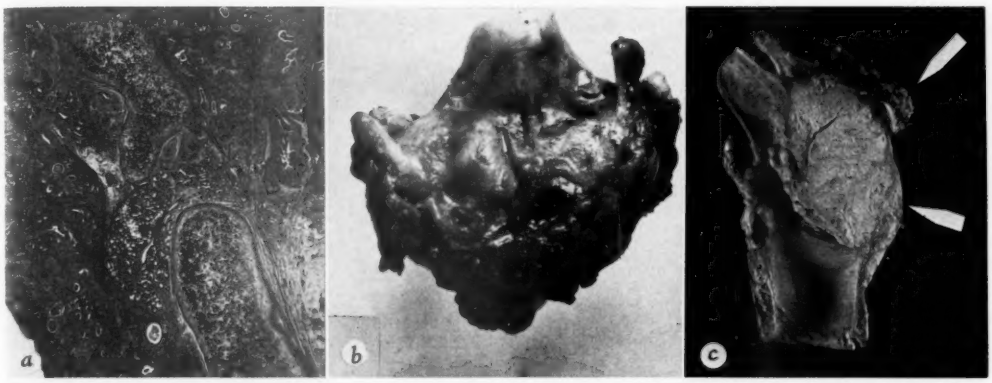

FIG. 2. Involvement of pre-epiglottic space by squamous carcinoma. A, microscopic infiltration of perichondrium, cartilage aperture and pre-epiglottic space. Hematoxylin and eosin stain, original magnification × 13. B, gross bulge due to tumor infiltration of pre-epiglottic space. Same specimen as Figure 1C. C, a sagittal section reveals the extensive involvement of this space.

Infiltrative Carcinoma. All the squamous cell carcinomas except the one described in the previous paragraph were of the infiltrative type. Examination of the fifty-six available laryngectomy specimens showed infiltration through the epiglottic cartilage in 80 per cent of the cases. The pre-epiglottic space was found to be involved microscopically in 75 per cent of these cases; this involvement ranged from penetration of the perichondrium on the anterior surface of the epiglottic cartilage to deep involvement of the areolar tissue filling the pre-epiglottic space and producing a gross bulge in the specimen. (Fig. 2.)

Ordinary Type. Various microscopic findings with particular features in the 114 infiltrating squamous carcinomas seem worthy of mention. (Figs. 3 and 4.) Thirty per cent of these cancers were of a so-called ordinary type. More than half of them were grade 2 lesions. The characteristic features of this type were hyperkeratotic, pseudopapillary surface and keratin cyst formation. (Fig. 3, A and B.) The hyperkeratotic superficial layer of malignant squamous cell formed wave-like undulations as well as sharply pointed structures which usually lacked the fine connective tissue cores seen in true papillary formations. This apparently accounted for the shaggy appearance of some of these tumors. Most keratin cysts were located just beneath the surface of the tumor, either at the base of pseudopapillary folds or in the superficial portion of the submucosa. Both keratin cysts and keratotic pseudopapillary formation were seen predominantly in grade 2 squamous cell cancers and were considered to be an expression of differentiation of the squamous carcinoma, similar to the epithelial pearls which also were abundant in these tumors.

Basaloid Type. Eight per cent of the squamous carcinomas were of the basaloid type. (Fig. 3, C and D.) Infiltrating squamous cells were obvious and, in addition, some of the nests and cords were composed of smaller, nonkeratinized cells, resembling those from the basal or parabasal layers of the mucosa. These nests often had a peripheral layer of cuboidal palisading cells, some of which formed numerous folds. These folds gave a ribbon-like or garland-like appearance to the lesion and Ringertz [1], one of us (D. K. S.) [2], and Shaw and Epstein [3] referred to this type as "transitional cell carcinoma." Similar basaloid type growths have been noted by Stout and Lattes [4] in squamous cell carcinoma of the esophagus. Although these growths usually were nonkeratinizing in the basaloid nests, occasionally they showed keratotic foci. A review of multiple sections of these tumors often showed additional zones which resembled ordinary squamous cell carcinoma. A brief summary of nine cases in which basaloid type carcinomas were present is shown in Table 1. Follow-up study showed local recurrence in two patients (Cases 1 and 11). Five year survival subsequent to initial treatment is included.

Other Types. One tumor was a true papillary growth with thin connective cores lined by multiple layers of squamous cells and with

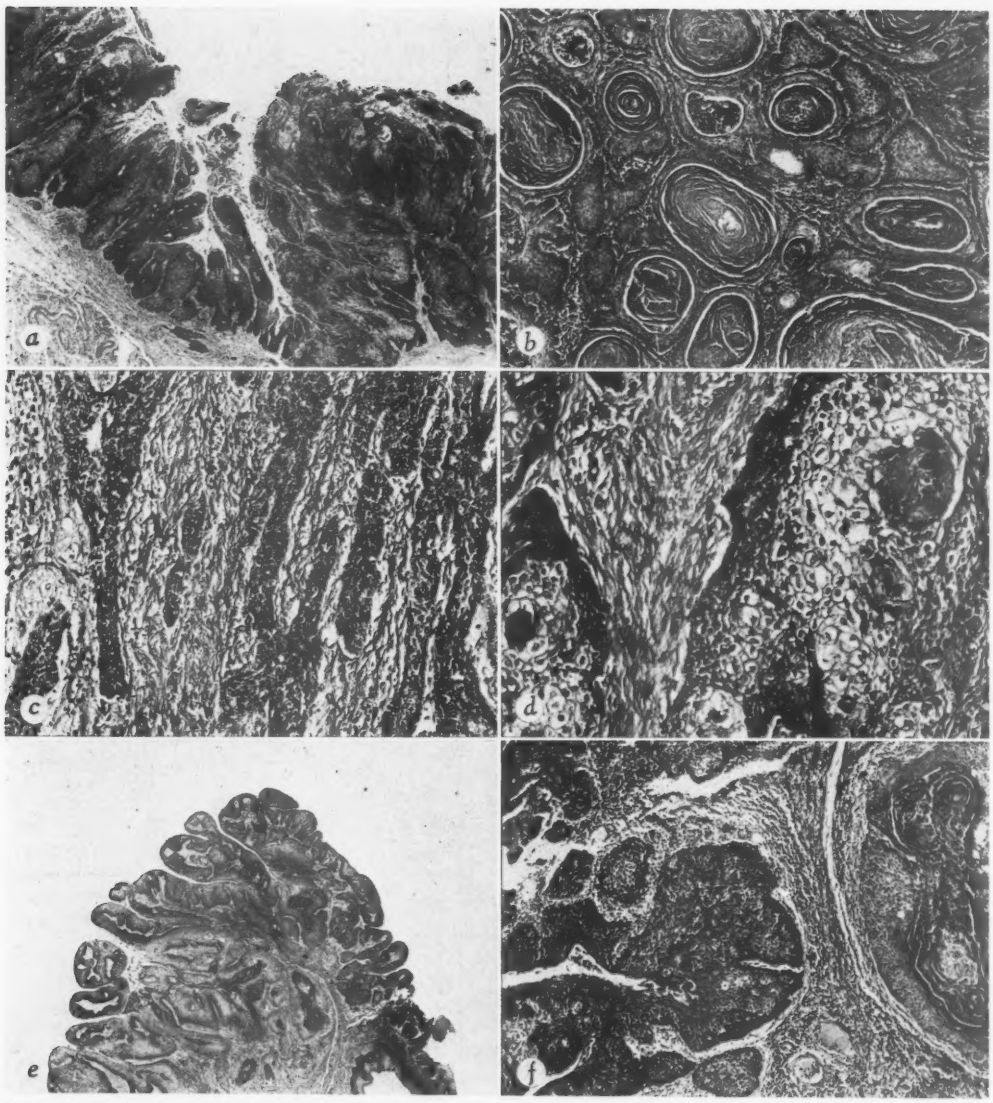

FIG. 3. Variations in microscopic appearance of squamous carcinomas of the epiglottis. Hematoxylin and eosin stain was used on all specimens. A, ordinary type showing a hyperkeratotic pseudopapillary surface. Original magnification × 13. B, ordinary type showing keratin cyst formation. Original magnification × 60. C, basaloid type showing essentially nonkeratinizing, ribbon-like cords of malignant cells. Original magnification × 145. D, basaloid type (same specimen as C) showing keratinizing foci. Original magnification × 175. E, papillary type showing papillary surface which superficially resembles papilloma. Original magnification × 12. F, papillary type (same specimen as E) showing infiltrating nests of squamous carcinoma. Original magnification × 60.

minimal keratin. (Fig. 3, E and F.) Parts of the growth superficially resembled squamous papilloma, yet evidence of malignancy was seen in anaplasia of the nuclei of squamous cells and nests of tumors were seen infiltrating into the submucosa.

The microscopic pattern of the one squamous cell carcinoma, grade 4, imitated that of a sarcoma. (Fig. 4.) Although the tumor was seen to arise from the mucosa, the malignant cells infiltrating the submucosa showed advanced spindling and anaplasia of nuclei with numerous mitotic figures, so that it had a sarcoma-like appearance, particularly where the cells infiltrated proliferating fibrous tissue. No examples of benign pseudosarcoma were found in this series.

The one adenocarcinoma in the series was located on the posterior surface of the epiglottis.

Four or 3.5 per cent of the squamous cell cancers were graded 1 (Broders' method), fifty-three or 46 per cent were graded 2, forty-five or 39 per cent were graded 3 and twelve or 10.5 per cent were graded 4.

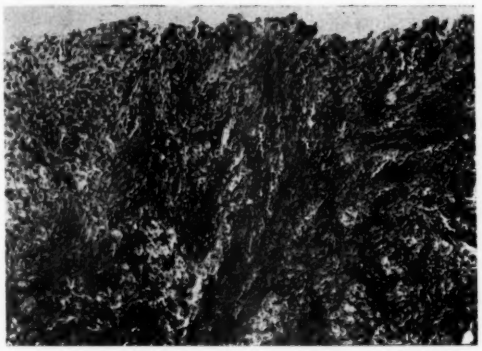

FIG. 4. Squamous cell carcinoma, grade 4, which microscopically imitated a spindling sarcoma. Hematoxylin and eosin stain, original magnification × 85.

METASTASIS

Twenty-eight per cent of 114 patients had significantly enlarged cervical lymph nodes on first examination. A record of these so-called significantly enlarged lymph nodes indicated that, in the opinion of the examining physician, who should be correct about 85 to 90 per cent of the time, the nodes were metastatic. In this series only eight of thirty-two patients with significantly enlarged lymph nodes on admission had surgical treatment. In seven of the eight patients, or 88 per cent of the cases, the examining physician was correct and the presence of metastasis was verified microscopically.

One patient also had metastasis to bilateral axillary lymph nodes. Six per cent of 114 pa-

TABLE 1

NINE CASES OF SQUAMOUS CELL CARCINOMA WITH BASAL CELL FEATURES

Case No.	Duration of Symptoms (months)	Lesion, Location and Grade	Initial Treatment	Treatment: Recurrence or Metastasis	Five Year Survival Since Initial Treatment
I	36	Combined, 2	External radiation	External radiation	Died of cancer
II	2	Laryngeal, 2	Laryngectomy	Right radical neck dissection; external radiation (nodes +)*	Lived 5 or more years
III	6	Laryngeal, 3†	Diathermy; external radiation	External radiation	Died of cancer
IV	11	Laryngeal, 2	Laryngectomy	...	Lived 5 or more years
V	7	Laryngeal, 2	Laryngectomy; external radiation	...	Lived 5 or more years
VI	6	Laryngeal, 3	Laryngectomy	No treatment	No follow-up
VII	3	Combined, 2	Laryngectomy	...	Lived 5 or more years
VIII	3	Combined, 2	Laryngectomy	Left radical neck dissection; external radiation (nodes +)	Lived 5 or more years
IX	8	Combined, 2	Laryngectomy	Right radical neck dissection (nodes −)	Lived 5 or more years

* (Nodes +) or (Nodes −) = histopathologic diagnosis.
† Bilateral cervical metastasis on admission.

TABLE II
SURVIVAL RATE IN RELATION TO GRADE AND SITE OF LESION AND CERVICAL METASTASIS

	Patients		Lived More Than 5 Years*	
	Total	Traced	No.	Per cent of Traced Patients
Grade				
1	4	3	3	100.0
2	53	48	31	64.6
3	45	42	19	45.2
4	12	12	4	33.3
Total	114†	105	57	54.3
Site				
Laryngeal	64	58	39	67.2
Lingual	17	15	3	20.0
Laryngopharyngeal	7	7	2	28.6
Combined	26	25	13	52.0
Cervical metastasis				
On admission				
Present	32	31	8	25.8
Absent	83	74	49	65.3
Over-all				
Present	56	52	18	34.6
Absent	59	53	39	72.2

* Inquiry as of January 1, 1958.
† The grade of the lesion was not mentioned in one case.

tients had significantly enlarged cervical lymph nodes bilaterally. So-called crossed metastasis was evident in only one lesion, a well-lateralized, grade 3 squamous cell carcinoma situated on the right side of the epiglottis. Biopsy specimen of the left supraclavicular nodes also revealed a grade 3 squamous cell carcinoma. The incidence of significantly enlarged cervical lymph nodes at the time of admission is highest among patients with lesions that involve the anterior or lingual aspect of the epiglottis. About a third of the patients whose cancers extended to the pyriform sinus or lateral wall of the pharynx had significantly enlarged cervical lymph nodes on admission.

Significantly enlarged cervical lymph nodes developed during the course of disease in approximately half of the 114 patients. Cervical metastasis developed during the course of disease in 42 per cent of the patients having laryngeal lesions, 70 per cent having lingual lesions, 43 per cent having laryngopharyngeal lesions and 50 per cent having the combined type. (Fig. 4.) It also developed in 25 per cent of the patients having grade 1 carcinomas, 43 per cent having grade 2 carcinomas, 51 per cent having grade 3 carcinomas and 75 per cent having grade 4 carcinomas. The higher the grade of malignancy and the closer the lesion was to the tongue or pharynx, the higher the incidence of cervical metastasis. In forty-three instances of proved microscopic invasion of the pre-epiglottic space, the incidence of cervical metastasis was 46 per cent. Metastasis to distant regions developed in about 5 per cent of the patients. The percentage seems low and is based on clinical findings after physical and x-ray examinations and one necropsy.

TREATMENT AND RESULTS

Of the 114 patients having squamous cell carcinoma of the epiglottis, 110 received treatment at the clinic. One hundred five could be traced. The survival rate for the 105 was 54.3 per cent. Survival rates in relation to three important factors, namely, grade, site and cervical metastasis, are shown in Table II. Treatment and results are shown in detail in Tables III and IV. The following types of treatment were used: (1) partial removal of the epiglottis (twenty-two patients); (2) laryngectomy (fifty-nine patients) and (3) radiation therapy (thirty-one patients).

Partial Removal of Epiglottis. Partial removal of the epiglottis was accomplished transorally in twenty-two patients by means of suspension laryngoscopy and by electrosurgery. In seven patients this treatment was supplemented with radon seeds inserted into the coagulated base of the wound; in three of the seven an average of 3,800 r was delivered through each lateral port with the 250 kv. machine. In five patients partial removal was supplemented with x-ray treatment alone (3,800 r to each side). This type of treatment has been abandoned except for the extremely early and small carcinoma on the mobile epiglottis (tip) in favor of transhyoid external removal of the epiglottis and dissection of the neck on one side. If the growth is lateralized, dissection is usually carried out on the side of the growth; if the growth is not lateralized or is exactly in the middle, dissection is carried

TABLE III

TREATMENT AND RESULTS BASED ON FIVE YEAR SURVIVAL (FREE OF DISEASE)

Chief Initial Treatment	Patients		Treatment		Results	
	Total	Traced	Initial Only	Plus Other Supplemental	Succeeded	Failed
Partial removal of epiglottis	22	20	5	15	10	10
Laryngectomy	57	53	36	17	28	25
Radiation	31	27	27	...	1	26
Radon seeds or radium needles	6	6	6	...	...	6
X-ray	12	9	9	...	1	8
Radon or radium plus x-ray	13	12	12	...	...	12
Total	110	100	68	32	39	61

out on the side which seems to contain the major portion or on any side, respectively.

We do not believe that the epiglottis and a large portion of adjacent anatomy can be removed with impunity. Older patients are more likely to have serious problems with swallowing than younger patients. It is safer to take part of the base of the tongue than it is to take both false cords or an arytenoid with the epiglottis. We do not intend to attempt the latter treatment. On occasion we have removed a false cord and part of the base of the tongue with the epiglottis, and in two instances we have had to resort to free-skin grafts to obtain satisfactory closure.

Of the twenty patients traced who had transoral removal of the epiglottis by means of suspension laryngoscopy, ten lived five years or more without recurrence or additional treatment. However, we did have to perform laryngectomy on one of the ten patients because of difficulty in swallowing. Eight of the remaining ten had additional treatment for cancer and five of the eight survived five years or more without recurrence. This additional successful treatment consisted of laryngectomy in one instance, dissection of the neck in two instances and implantation of radon seeds for metastatic cervical lymph nodes in two instances. Of the twenty patients traced who had transoral removal of the epiglottis, fifteen survived five years or longer which gave a survival rate of 75 per cent for the twenty patients traced and of 68 per cent for the entire group of twenty-two.

Laryngectomy and Neck Dissection. From 1950 to 1952, narrow-field laryngectomy was abandoned in favor of wide-field laryngectomy in combination with unilateral or bilateral neck dissection depending on the clinical setting. During most of the years covered by this study, neck dissections rarely were performed even therapeutically. Radon seeds usually were implanted in metastatic nodes and the patients were treated with a 250 kv. machine. Any

TABLE IV

RESULTS OF ADDITIONAL TREATMENT FOR FAILURES: FIVE YEAR SURVIVAL FREE OF DISEASE SINCE DATE OF LAST PROCEDURE

Types of Treatment	Failures		Results After Added Treatment	
	Total	With Added Treatment	Success	Failure
Partial removal of epiglottis	10	8	5	3
Laryngectomy	25	19	8	11
Radiation	26	15	1	14
Radon seeds or radium needles	6	6	1	5
X-ray	8	3	0	3
Radon or radium plus x-ray	12	6	0	6
Total	61	42	14	28

improvement in over-all results should occur in the group of patients having metastatic lesions in the neck. Many patients who were considered inoperable and who once were referred for radiation therapy should now be treated surgically.

Of the fifty-three patients traced who had laryngectomy, twenty-eight survived five years or longer without recurrence or additional treatment. Only six of the twenty-eight patients had dissection of the neck as part of their initial treatment. Of the other twenty-five of the fifty-three patients, nineteen had additional treatment for cancer and of these nineteen, eight survived five years or longer without recurrence. This additional successful treatment consisted of neck dissection in seven instances, and x-ray therapy in one instance. Of the fifty-three patients traced who had laryngectomy, thirty-six survived five years or longer, a survival rate of 68 per cent for the fifty-three patients traced or 63 per cent for the total number of fifty-seven.

Radiation Therapy. A rather curious change has developed in the utilization of radiation therapy for cancer of the larynx. Some years ago it was used in far advanced cases or the extremely poor risk patient with the rather forlorn hope that the patient might get well. With the advent of cobalt (Co^{60}) therapy at the clinic, we have gradually reversed our ideas regarding radiation versus surgical therapy for this condition. Now, we are much less reluctant to use radiation in the early superficial cancer of the larynx than formerly, while surgical procedures are used almost to the exclusion of radiotherapy in the moderately to far advanced cases. Cobalt therapy is used occasionally for superficial cancer of the epiglottis if the clinical setting is right. In general, however, there is little question in our minds that surgical treatment, whether it be amputation of the epiglottis or laryngectomy with neck dissection, is the procedure of choice.

Laryngectomy and neck dissection after radiation failure can be accomplished but problems of postoperative sloughing, hemorrhages and formation of fistulas are encountered. Laryngectomy, however, was accomplished after radiation failures in eight patients with good results in four.

Of the twenty-seven patients traced who had radiation therapy, one survived five years or longer without recurrence or additional treatment. Of the other twenty-six patients whose condition was traced, fifteen had additional treatment for cancer and of these one survived five years or longer without recurrence. This one success was accomplished with laryngectomy, the only case in this group in which it was attempted. Of the twenty-seven patients traced who had radiation therapy, therefore, two survived five years or longer, a survival rate of 7 per cent for the twenty-seven patients traced or 6 per cent for the total thirty-one patients.

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Total Laryngectomy and Cervical Esophagectomy

RECONSTRUCTION EMPLOYING A GREATER CURVATURE GASTRIC TUBE

JOHN C. HAWK, JR., M.D., *Charleston, South Carolina*

From the Cancer Clinic and the Department of Surgery of the Medical College of South Carolina, Charleston, South Carolina.

THE NUMBER AND VARIETY of procedures described for restoration of alimentary continuity following laryngo-pharyngectomy and/or cervical esophagectomy attest to the magnitude of the problem and the lack of a uniformly satisfactory solution. Several extensive reviews of the subject have appeared in the literature in recent years [*1–4*]. When sufficient pharyngo-esophageal mucosa remains, primary reconstruction may be feasible, but when more radical resection has been required it becomes necessary to employ more complicated measures. Among the methods which have been advocated are these:

1. The Wookey [*5*] two stage reconstruction, using a laterally based, full thickness skin flap.

2. The use of more extensive tubed pedicle grafts as described by Bricker and Burford [*6*].

3. One stage reconstruction by means of a split thickness skin graft supported by a stent, such as the tantalum or stainless steel mesh framework described by Edgerton [*7*] or the polythene tube employed by Reidy [*8*].

4. The use of a long small bowel loop or a segment of colon as a conduit from hypopharynx or cervical esophagus to stomach. These visceral conduits have been placed intrathoracically, retrosternally or in a prethoracic subcutaneous skin tunnel, in various modifications by several authors, including Mahoney and Sherman [*2*], Beck and Baronofsky [*3*], Goligher and Robin [*4*], Jentzer [*9*] and Petrov [*10*].

5. The employment of the stomach itself, mobilized in a variety of ways and brought to the neck by any one of the three routes described here: intrathoracic, retrosternal or subcutaneous [*1,11–15*]. A recent report by Ong and Lee [*12*], for instance, cites three cases of pharyngogastric anastomosis, with the stomach brought transthoracically by means of abdominal, right thoracic and cervical approaches.

The Wookey procedure and the tubed pedicle grafts have the disadvantage of requiring multiple-staged procedures. Both these and the one stage reconstruction by split thickness graft over a stent are limited by the necessity of having a sufficient length of thoracic esophagus available at the base of the neck to permit secure anastomosis. Although a small bowel loop may be used without special preoperative preparation, the employment of either the right or the left colon requires adequate preoperative cleansing and makes this method unsuitable when "impromptu" reconstruction is required because of more extensive disease found at the time of operation.

Of the various methods utilizing the stomach, the use of a greater curvature tube attached near the cardia has seemed the most feasible to us. The procedure, although previously described as far back as 1905 by Beck and Carrell [*16*], and in 1912 by Jianu [*17*], was brought again to attention by the work of Heimlich and Winfield [*13*] in 1955 and by the independent work of Gavriliu in Bucharest [*14*]. In 1959 Heimlich [*15*] reported ten cases in which he employed this "reversed" gastric tube for esophageal replacement and cited the more extensive experience of Gavriliu, which included one case of resection of the larynx, pharynx and cervical esophagus.

DESCRIPTION OF PROCEDURE

The procedure is diagrammed in Figure 1. A left subcostal incision is used. The spleen is

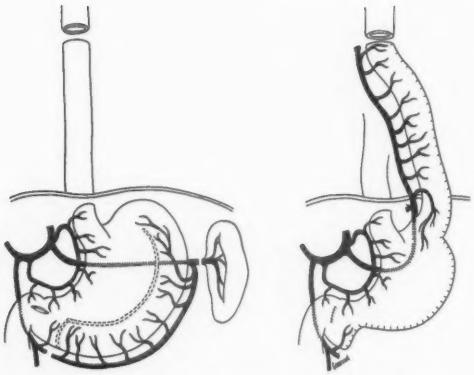

FIG. 1. Formation of "reversed" gastric tube from greater curvature of stomach (after Heimlich). Note removal of spleen, preservation of left gastroepiploic vessels, mobilization of splenic artery (with body and tail of pancreas) and performance of pyloroplasty (omitted in the case reported).

removed, taking care to preserve the left gastroepiploic vessels. The body and tail of the pancreas are mobilized. A tube, approximately 3 to 4 cm. in diameter, is made from the greater curvature of the stomach, which is allowed to remain attached at the cardia. This reversed gastric tube is carried cephalad through a subcutaneous tunnel to the neck, for anastomosis to the cervical esophagus or pharynx. An adequate length to reach the base of the tongue can readily be obtained. Pyloroplasty should be performed and gastrostomy is employed for temporary feeding. Although a retrosternal course may be employed for the tube, the prethoracic subcutaneous position is preferred as being safer in case of any transient leakage. Avoidance of entry into the thoracic cavity lessens the magnitude of the procedure and makes it better tolerated by the patient.

This method had previously been employed by us for the palliative bypassing of obstructing carcinomas of the thoracic esophagus, and in one case for reconstruction after resection of a carcinoma of the cervical esophagus, which had recurred after radiation therapy. The patient in the latter case is now surviving and well forty-five months after original diagnosis and thirty-nine months following resection. The suitability of the method for application following total largyngo-pharyngectomy and cervical esophagectomy became apparent in the case presented here.

CASE REPORT

J. P. T., a sixty-nine year old white college janitor and handyman, was admitted to the Medical College Hospital, Charleston, South Carolina, on February 13, 1958, with a complaint of pain in his throat for three months. Symptomatic treatment by his dentist, a chiropractor and his family physician had provided no relief. One week prior to admission a diagnosis of carcinoma of the left pyriform fossa was made by an otolaryngologist.

Examination on admission showed the entire left pyriform fossa to be filled with a granular mass, pushing the edematous left arytenoid well beyond the midline. The glottic opening was obscured by the overhanging left arytenoid but the right half of the larynx appeared to move satisfactorily. A 2 by 1.5 cm. rubbery node was located just below the left carotid bulb.

A soft tissue x-ray film of the cervical region indicated the extent of the primary lesion. Barium swallow likewise outlined the large soft tissue mass of the left pyriform fossa but showed no other lesions. X-ray examination of the chest showed negative results. Biopsy of the lesion of the left pyriform fossa was reported to show epidermoid carcinoma of grade 2 activity.

On February 17, 1958, left radical neck dissection was carried out, allowing the specimen to remain attached to the larynx and left half of the hypopharynx. When the hypopharynx was entered on the right side, away from the primary lesion, an area of superficial keratosis, suggestive of early carcinoma, measuring 1 cm. in diameter, was noted in the right pyriform fossa. Frozen section of the excised small lesion was reported as probable carcinoma, although invasion was not conclusive. Total laryngectomy was then carried out in continuity with the radical neck dissection. At this time visualization of the cervical esophagus was feasible for the first time and a third separate lesion was noted on the posterior wall of the cervical esophagus, biopsy of which showed invasive epidermoid carcinoma on frozen section study. Esophagoscopy was carried out, showing the lesion to extend 7 cm. below the level of the cricopharyngeus. Distal to this point the esophagus appeared normal.

At this time it was decided to proceed with resection of the entire hypopharynx, cervical esophagus and the upper portion of the thoracic esophagus as far as could be reached through the thoracic inlet. A margin of at least 3 cm. beyond the lesion was obtained. The distal segment of the esophagus was inverted as a blind end, closed with two layers of interrupted sutures. When released, it retracted approximately to the level of the carina.

The neck wound was temporarily covered, the abdomen and thorax exposed and a greater curvature gastric tube fashioned as described here. This was brought through a subcutaneous antethoracic tunnel and was anastomosed to the base of the tongue, the posterior pharyngeal wall and the tonsillar pillars. While the cervical anastomosis was being carried out by the operator, a second team performed a Stamm gastrostomy and closed the abdominal incision.

Two avoidable complications occurred. The first became apparent as the procedure was concluded, when large quantities of air were noted to dissect beneath the cervical skin flaps. A tear in the posterior wall of the trachea was found approximately 2 cm. above the carina. This had apparently resulted from overdistention of the endotracheal tube balloon in an area weakened by dissection of the trachea from the esophagus. Several attempts to close the opening by suturing through the tracheostome were only partially successful and finally a long laryngectomy tube was employed to go beyond the rent. With suction applied to catheters beneath the skin flaps, further dissection of air was controlled.

The second complication appeared on the eleventh postoperative day when tube-feeding material appeared in the trachea; it became evident that there had been regurgitation of fluid up the remaining distal esophagus from the stomach, with establishment of a temporary tracheo-esophageal fistula in the area of the rent in the trachea. Suction was applied to the gastrostomy tube, parenteral alimentation was given temporarily and subsequently feedings were administered through a Miller-Abbott tube inserted through the gastrostomy past the pylorus and into the jejunum. This complication could have been avoided by performance of pyloroplasty at the time of operation and by more cautious administration of gastrostomy feedings.

On the twenty-first postoperative day the patient was started on oral liquid feedings, progressing to a soft diet. He was discharged on his twenty-seventh postoperative day, taking soft foods without difficulty.

The Pathology Department reported three separate carcinomas. The lesion of the right pyriform fossa was considered questionably invasive, while the larger lesions in the left pyriform fossa and cervical esophagus were definitely invasive. Findings in the lymph nodes were negative for metastases.

The anastomosis at the base of the tongue required dilatation on one occasion in May 1958. This was readily effected by having the patient swallow a no. 30 Foley catheter, which was then withdrawn slowly several times after inflating the bulb each time with 2 to 3 cc. of air. Two suture granulomas were removed from the neck at the same time.

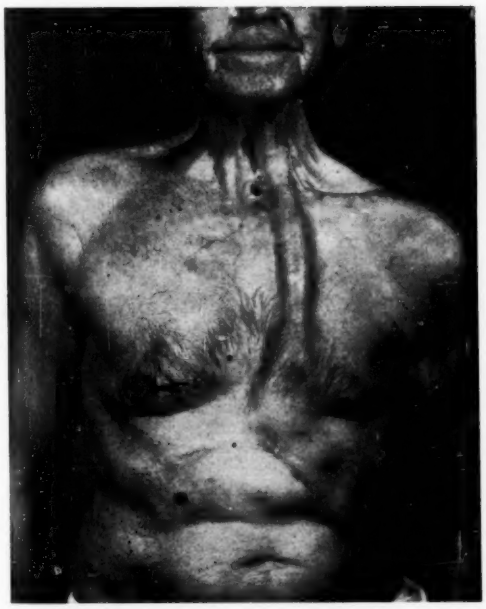

FIG. 2. Patient J. P. T. in March 1961, thirty-six and a half months after resection of larynx, pharynx and cervical esophagus for three separate primary lesions. Note subcutaneous gastric tube reaching to base of tongue.

The patient was last seen on March 4, 1961, and remains free of recurrence three years after operation. He has had bilateral inguinal herniorrhaphies since his original operation and at the present time has symptoms of prostatism but otherwise is getting along well. He is a bachelor, lives alone and does all his own cooking and housework. His physical appearance in March 1961 is shown in Figure 2.

COMMENTS

The accurate determination of the extent of lesions of the hypopharynx and larynx is essential to the proper planning of an operative procedure suitable for a given case. The presence of a bulky lesion in the hypopharynx may, however, preclude completely accurate evaluation either by mirror or by endoscopy. Soft tissue x-ray examinations of the neck, barium swallow and laminograms are useful but may not delineate completely a superficial or small separate lesion.

The finding of two additional unsuspected primary lesions in this case necessitated more

radical resection than had been anticipated. The low transection of the esophagus, actually within the upper thorax, precluded the use of the Wookey procedure, tubed pedicle grafts or the Edgerton procedure. Furthermore, the skin incision had not been specially planned for the Wookey procedure. The large bowel had not been suitably prepared for use. Thus employment of a loop of small bowel or of the stomach provided the best method for primary reconstruction. This was readily carried out by the use of a reversed greater curvature gastric tube. The first complication cited above could certainly have been prevented by greater care in inflation of the endotracheal balloon, and the second by performance of pyloroplasty, which is now routine.

SUMMARY

A case is reported in which the finding of an additional primary carcinoma of the right pyriform fossa and one of the cervical esophagus at the time of left radical neck dissection and laryngectomy for carcinoma of the left pyriform fossa necessitated resection of the entire hypopharynx, cervical esophagus and a portion of the upper thoracic esophagus. Satisfactory primary reconstruction was effected by employing a reversed, greater curvature, gastric tube brought through a subcutaneous antethoracic tunnel and anastomosed to the base of the tongue, posterior pharyngeal wall and tonsillar pillars. A three-year follow-up of the patient who was free of recurrence is described.

Various other methods of reconstruction following resection of the cervical esophagus, larynx and hypopharynx are reviewed briefly and reasons are cited for the preference of the method employed in this particular case.

Acknowledgement: I am indebted to Dr. Forde A. McIver, of the Department of Pathology of the Medical College of South Carolina, for performing the multiple frozen section studies.

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Treatment of Advanced Tongue Cancer by Suprahyoid Total Glossectomy and Excision of Floor of the Mouth

MARCEL DARGENT, M.D., *Lyon, France*

From the Centre Leon Bernard, Lyons, France.

CLINICALLY SPEAKING, there is a group of mouth cancers whose dominant characteristic is massive local involvement of submucosal and deep musculature of the tongue unassociated with clinical invasion of adjacent structures. In particular, the mucosa of the floor of the mouth, gums, and glosso-epiglottic fold remain free of cancer. The mandible itself is usually normal by roentgenogram and the lymph nodes of the neck are clinically uninvolved.

Radiation of this type of tumor has been unsatisfactory because of the large mass of tissue to be treated. The use of interstitial radium needles risks radionecrosis and presents the difficulty of securing an effective homogeneous dose. Therefore, with radiation therapy, pain remains a prominent symptom and little palliation is secured. On the other hand, this mass that is bounded anteriorly and laterally by the concavity of the mandible, inferiorly by the hyoid bone and posteriorly by the epiglottis is surgically resectable. I believe this concept has prompted me to attempt this type of excision in five patients.

PRELIMINARY PROCEDURES

Surgery of this magnitude demands that two preliminary procedures be carried out in order to assure an adequate airway and provide for nourishment. The first of these is tracheostomy which is absolutely necessary in order to accomplish safely the operative excision and avoid postoperative pulmonary complications. The second procedure is a gastrostomy. Although there may be some disagreement on the necessity for this particular operation, I agree with Gardham who emphasizes the danger of the indwelling esophageal catheter as a source of respiratory infection. Gastric regurgitation provoked by a gaping cardioesophageal sphincter and encouraged by secondary irritation of the laryngeal mucosa from prolonged close contact with a rubber catheter can lead to aspiration pneumonia. These two preliminary procedures, tracheostomy and gastrostomy, are carried out one week before the main operation. During this period the patient receives supportive therapy with vitamins and antibiotics.

Anesthesia. The young and healthy patient can be operated on under general anesthesia induced by nesdonal and maintained on ether endotracheal inhalation. In patient considered a poor risk, and particularly in the chronic alcoholic in whom biopsy of the liver at time of gastrostomy has demonstrated a precirrhotic state and warned of the possibility of postoperative acute delirium tremens, I prefer to use local and regional anesthesia with Scurocaine® 1 per cent. The suprahyoid region is infiltrated with the anesthetic solution, while the inferior maxillary nerves are blocked at their point of exit from the skull. Preoperative sedation with a mixture of Dolosal® (pethidine), Phenergan® (promethazine) and Largactil® (chlorpromazine) is given parenterally two hours before surgery. This sedation seems to provide the best prevention of delirium.

SURGICAL PROCEDURE

The purpose of the operation is to remove the cancer, preserving the mandibular arch and restoring the floor of the mouth by means of a free skin graft applied to the raw posterior

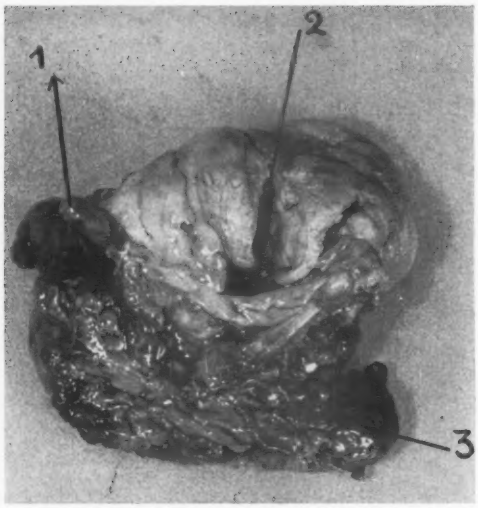

FIG. 1. Operative specimen. (1) Hyoid; (2) tumor of the base of the tongue; (3) supra-hyoidian structures.

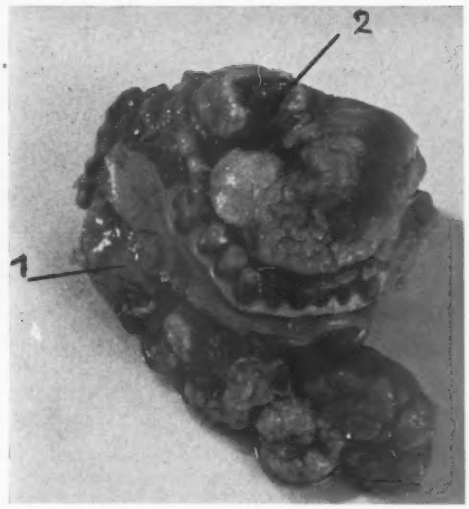

FIG. 2. Operative specimen. (1) Hyoid; (2) base of the tongue.

surface of the skin of the neck. If the superior laryngeal nerve can be preserved, thereby maintaining normal sensation to the larynx, the larynx need not be sacrificed. The constrictor muscles of the pharynx are usually undamaged by tumor invasion and can be saved, thereby making it possible for the patient to learn how to swallow.

SURGICAL TECHNIC

The preferable incision must spare the soft tissue of the chin and should therefore be made horizontally at the level of the hyoid bone or slightly above it. At each lateral extremity of the incision near each angle of the mandible, a small vertical incision is made to facilitate reflection of the flap to the level of the lower lip.

It is important to avoid vertical incisions in the chin flap so that the flap will be a better recipient for the skin graft to be used in the restoration of the floor of the mouth. However, if a vertical incision seems mandatory in the patient with a short, thick neck, then it may be employed but not in the lower lip. The flap should include the platysma muscle so that the blood supply to the skin will be abundant.

In raising the flap, it is essential to demonstrate and isolate on each side the ramus marginalis branch of the seventh nerve. The preservation of this nerve is very important as it will assure the patient of good closure of the mouth, which is the first step in deglutition. When the flap has been reflected to the level of the mandible, the facial vessels on each side are isolated, ligated and divided. The superficial cervical aponeurosis is divided on each side at the level of the hyoid bone, the incision extending laterally to the anterior border of each sterno-mastoid muscle. At this point the facial vessels are again encountered inferior to the posterior belly of the digastric muscle. These vessels are again ligated and divided, after which the tendon of the digastric muscle is divided, exposing and sacrificing the hypoglossal and lingual nerves and the lingual vessels.

The muscles along the inferior edge of the hyoid bone are transected and the scissors are then used to divide the thyroglosso-epiglottic fold. At this time it is easy to detach the tongue musculature from the genioid process and mylohyoid ridge of the mandible. The incision is made in the buccal mucosa as close as possible to the gingiva, and then extended posteriorly to the lower pole of each tonsillar fossa. From this point it passes medially until it joins the incision at the glosso-epiglottic fold. Thus, the removal of the whole tongue *en bloc*, with its suprahyoid musculature and hyoid bone, is carried out. (Fig. 1.)

Some modifications are possible. When

significant node involvement is present in the cervical area, a block dissection of the neck on the affected side is undertaken at the same time. If the local extension of the tongue cancer reaches the gum, a marginal resection of the superior portion of the mandible is performed. The bone is sawed as in the "pull through operation" (Ward-Slaughter) and a thin inferior bony rim is preserved. (Fig. 2.)

CLOSURE

The large flap is sutured to the inferior edge of the mandible with interrupted chromic catgut passing through platysma and mandibular periosteum. Before applying the free skin graft to the platysmal surface of the neck flap, it is advisable to divide the platysma and subcutaneous tissue for about 2 cm. in width along the inferior edge of the neck flap. The skin graft is sutured to the superior portion of the flap, and the inferior margin of the skin graft is sutured to the mobilized anterior mucosa of the epiglottis and the lateral aspects of the extrinsic larynx. The remainder of the neck flap, which is uncovered by skin graft, is sutured to the skin of the neck, thereby providing a skin closure that does not coincide with the skin graft closure that is bathed in saliva. This separation of the closure lines is a safeguard against development of a salivary fistula. The most lateral parts of the neck flap are sutured to the pharyngel wall, the skin graft being sutured to pharyngeal mucosa. The end result is an epithelial-lined buccal cavity, with the epiglottis occupying a more anterior

FIG. 3. The result after one year: epiglottis is drawn up in the oral cavity.

position at the former site of the midtongue. (Fig. 3.) The external appearance, due to preservation of mandibular contour, is excellent. (Fig. 4A and 4B.)

POSTOPERATIVE CARE

A block dissection of both carotid areas is undertaken two or three weeks later. Tracheostomy and gastrostomy are usually unneces-

4A 4B

FIG. 4. The patient six months after the operation. A, lateral view; B, anterior view.

sary after six weeks. In the first week a gauze plug soaked in Aureomycin® powder is placed within the oral cavity once a day. At the end of the second week the patient is allowed nourishment by mouth. In the beginning, aspiration into the larynx, followed by violent coughing, is common. However, with encouragement and perseverance, this is overcome and deglutition returns. For the first two or three months speech is poor and only labial consonants are understood. As time passes, the patient learns to use his lips and cheeks in speaking, and his speech becomes intelligible.

CASE REPORTS

CASE I. A forty-nine year old man was admitted on December 12, 1955 with a four months' history of unsuccessful treatment of a tongue cancer by ointments and external and interstitial radiation. The right external carotid artery had been ligated because of recurrent hemorrhages. Pain radiating to the ears was a prominent symptom. Examination revealed the base and middle third of the tongue to be replaced by a deep necrotic ulceration. The glosso-epiglottic fold was free; there was no evidence of cervical node metastasis. X-ray examination of the mandible did not demonstrate tumor involvement. On January 7, 1956, after preliminary tracheostomy and gastrostomy, exenteration of the mass through the floor of the mouth and reconstruction by skin graft was carried out. The pathology report showed anaplastic spindle cell carcinoma. On April 13, 1956, the gastrostomy was closed and the patient was in good condition, able to swallow and free of pain. On May 12, there was a large local recurrence of cancer in the right tonsil. There was no metastasis in the neck. Late in May the patient died from a sudden hemorrhage.

CASE II. A forty-two year old man, with chronic alcoholism, was admitted on October 19, 1956 with a history of an untreated tumor in the floor of the mouth. Examination revealed a large diffuse ulcer involving the right mid one-third of the tongue, crossing the midline to involve the left mid one-third, with extension into the entire anterior one-third of the tongue and the floor of the mouth on both sides. Posteriorly the disease extended to within 3 cm. of the glosso-epiglottic fold.

On November 3, after preliminary tracheostomy and gastrostomy, the tumor was excised by the previously described technic combined with a marginal resection of the superior aspect of the mandible. The superior laryngeal nerves were demonstrated and preserved on both sides. The operation was uneventful. Postoperatively a salivary fistula developed but closed spontaneously in six weeks. On November 24 and subsequently on December 1, neck dissections were carried out. A submaxillary lymph node on one side was reported as "spindle cell carcinoma with anaplasia." On February 25 feeding by mouth was possible despite some trismus. Speech was poor. On June 14, 1957, there was widespread local recurrence in the mouth and neck and on July 6 the patient died from hemorrhage.

CASE III. A forty-six year old man was admitted on February 7, 1957 with a three year history of unsuccessful attempts to control a floor of mouth cancer by local excision and external and interstitial radiation in a hospital at Beziers. Examination revealed a fistulous abscess in the submental area and diffuse neoplastic involvement of the entire tongue and deep musculature. The glosso-epiglottic fold was free and there was no clinical evidence of node metastasis.

After tracheostomy and gastrostomy on February 12, under local anesthesia, excisional surgery under local and regional anesthesia was carried out on February 18. The pathology report showed spindle cell carcinoma of the tongue. Postoperatively a fistula developed in the submental area. On June 18, the fistula had almost closed and feeding by mouth was possible. Accordingly, the gastrostomy was closed. The patient at that time had gained 5 kg. In October 1957, there was diffuse recurrence in the mouth and neck. Trismus was of such a degree that it was necessary to reopen the gastrostomy. The patient died in December 1957.

CASE IV. A sixty-three year old man was admitted on April 29, 1957, having been treated previously by me with external and internal radiation. Examination revealed the recurrence of a large, ulcerated infected area involving the entire base and left side of the tongue with fixation to the floor of the mouth. A node was palpable in the submental area in the midline. After gastostomy and tracheostomy on May 6, 1957, excisional surgery was carried out on May 9, 1957. The pathologic report showed spindle cell carcinoma with metastasis to the lymph nodes of the submental area. Postoperatively the skin flap sloughed, producing a large fistula in the left neck. A large, tubed pedicle skin flap was formed on the anterior chest wall and migrated to fill the defect in three stages (June 4, July 27, and October 26, 1957). On February 9, 1958, pulmonary metastasis was demonstrated.

CASE V. On November 3, 1957, a thirty-seven year old woman was admitted to the Department of Radiotherapy for treatment of a tumor of the tongue of twelve months' duration. There had been no previous treatment. Examination revealed a bulky tumor involving the middle third of the

tongue with ulceration of the left side of the tongue and fixation to the floor of the mouth. The glosso-epiglottic fold was free and there was no evidence of lymph node metastasis. A biopsy showed adenocarcinoma, with some portions showing trabecular and secretory components.

The patient was treated with telecobalt from November 5, 1957 to February 13, 1958, receiving a tumor dose of 4,075 r. There was slight improvement in mobility. In March 1958, pain increased and feeding was impossible. On March 21, 1958, gastrostomy and tracheostomy were carried out and on March 31, 1958, the tumor was excised by the previously described technic. The pathologic condition was reported as residual and recurrent adenocarcinoma. The nodes were not involved.

Postoperatively a small fistula occurred but closed spontaneously at the end of the second week. The tracheostomy was closed on the twenty-third postoperative day and on May 21, 1958, the gastrostomy was no longer needed. Speech was intelligible and oral feedings were easily taken. On September 26, 1958, there was metastasis to the left cervical lymph nodes and on October 7, 1958, a radical neck dissection was carried out. The pathologic condition showed metastatic adenocarcinoma to the lymph nodes of the upper portion of the neck.

In May 1959 following an upper respiratory infection, edema of the face and neck developed. Oral examination failed to reveal gross recurrence but smears of the oral mucosa were reported as Papanicolaou Class 5, consistent with diffuse local recurrence of the cancer. Despite chemotherapy and antibiotic therapy, the patient died in December 1959 of cachexia.

SUMMARY AND CONCLUSIONS

The procedure of exenteration of the tongue and floor of the mouth through a suprahyoid approach preserving the mandibular arch and the larynx is reserved for carefully selected cases. The presence of skin involvement in the submental region, the presence of clinically obvious metastatic lymph nodes in the neck and involvement of the glosso-epiglottic fold are contraindications for the procedures. Five of these operations have been performed with no operative or postoperative deaths resulting. There were four fistulas; three of these were small, did not prevent oral feedings and healed spontaneously. Only one of the fistulas required secondary closure.

From the technical point of view, removal of the depressor muscles of the mandible may lead to the trismus that was demonstrated postoperatively in some of the cases. Perhaps in the future it would be wise to divide the masseter and pterygoid muscles to avoid this complication. As already mentioned, preservation of the ramus mandibularis nerves to insure closure of the lips and preservation of the superior laryngeal nerves to protect sensation of the respiratory tract are steps that are absolutely essential if acceptable function is to be secured.

Follow-up studies have shown that failures have been due to diffuse local recurrencé in the mouth and neck. Except in one instance, I have not witnessed recurrence in a mandible.

The poor final results seem to be a reflection of the far-advanced state of local disease when surgery was performed, and yet I am reluctant to extend the surgical boundaries to encompass more areas than are at the site of local recurrence. Such action would result in a greater deformity which would, in my opinion, probably produce no greater success.

If this procedure is to result in any patients surviving for long periods, it must be performed in all patients presenting the described indications and in whom previous treatment has been unsuccessful. In such a group of patients one can expect to secure fairly good function and satisfactory palliation.

Cavernous Hemangioma of the Oral and Hypopharynges

EDWIN W. COCKE, JR., M.D., *Memphis, Tennessee*

From the Department of Otolaryngology, The University of Tennessee College of Medicine, Memphis, Tennessee.

CAVERNOUS HEMANGIOMA of the pharynx is a very rare disease. It is the purpose of this paper to review the literature that pertains to this subject and to report one additional case. Nine cases of hemangioma of the pharynx, exclusive of angiofibroma of the nasopharynx and hemangioma of the tonsil, have been recorded in the English literature since Wolfenden [1] reported the first case in 1887. Included in this series is one hemangioma of the right tonsillar fossa reported by Trible [2] in 1927. It was assumed that this tumor arose from the pharyngeal wall since examination of the patient failed to reveal evidence of tonsillar tissue.

AGE, SEX AND RACE

The median age of the patients reported in this series was twenty-five years. The youngest was seven and the oldest fifty-five years of age. Four of the tumors occurred in men and two in women. The sex of three patients was not recorded. Although the race of each patient was not recorded, none of the tumors reported occurred in Negroes.

SYMPTOMS

The symptoms manifested by these patients were directly related to the size, location, degree of ulceration and secondary infection of the tumor. Dysphagia occurred in five patients. The severity of symptoms varied from a vague feeling of fullness in the throat to marked difficulty in swallowing. One patient was asymptomatic even though the tumor was large enough to occupy the entire right half of the oropharynx. Two of the patients had dyspnea. In one instance a tracheostomy was necessary. Hoarseness and/or a change in voice developed in three patients. Cough and pain occurred in one each. Four patients noted at least some degree of bleeding. This symptom manifested itself as blood-streaked sputum. In one instance as much as a teacup full of blood was expectorated. Bilateral mucopurulent nasal discharge was a prominent symptom in one patient with soft palate and uvula involvement.

DURATION

Since some of the tumors did not produce symptoms, it is difficult to determine with any degree of accuracy the duration of the disease. In the twenty year old patient the writer was certain that the tumor had been present since birth. In the seven and ten year old patients, New and Childrey [5] indicate that the lesions had produced symptoms for a "few months to years." Symptoms had been noticed for six months in the fifty-five year old patient [6], for one year in the forty-five year old patient [7] and for twelve years in the forty-eight year old patient [3]. One twenty-five year old patient was asymptomatic [1]. The duration of the symptoms was not recorded in two patients.

PHYSICAL SIGNS AND LOCATION OF THE TUMORS

The appearance and location of each tumor was quite characteristic of a cavernous hemangioma of the pharynx even though contiguous pharyngeal structures were occasionally invaded by the disease. Each tumor was elevated, smooth-surfaced, glistening, circumscribed and occasionally lobulated. Two of the tumors were soft and one was firm. The color varied from red to dark blue. Large, dilated veins extended from the peripheral border of only one tumor into the adjacent soft tissues. None of the tumors exhibited pulsation. The size of the

tumors varied. The smallest was reported by Walford [6] in 1931. It was "pea-sized." The largest was reported by Woodward [3] in 1936. It extended from the soft palate to the esophagus. "Walnut-sized" and "peanut-sized" tumors were reported, respectively, by Trible [2] and Lillie [7].

Four of the tumors were confined to the oropharynx. One involved the right tonsillar fossa [2] and another involved the upper, posterior oropharyngeal wall [5]. In Lillie's [7] case the left lateral pharyngeal band was involved from the nasopharynx to the lower pole of the tonsil. Wolfenden [1] reported a similar lesion involving the right lateral and posterior walls of the pharynx from the level of the soft palate to the level of the base of the tongue. This tumor involved the right lateral pharyngeal wall and extended medially to beyond the midline of the pharynx.

Three of the lesions primarily involved the hypopharynx. Two of these arose from its posterior wall. One was "pea-sized" at the level of the arytenoid cartilage [6] and the other was perhaps larger [7]. A third hypopharyngeal tumor involved the left lateral wall of the pharynx, the pyriform sinus and false and true vocal cords [4].

One of the hemangiomas was located in the oral and hypopharynges [8]. It involved each tonsillar fossa, the right base of the tongue, the epiglottis, each pyriform sinus, ventricular bands and ventricles.

The largest tumor primarily involved the oropharynx and larynx. The soft palate, uvula, anterior and posterior tonsillar pillars, base of the tongue, epiglottis, arytenoid, true and false vocal cords were involved on the right. The left arytenoid, anterior and posterior commissures of the larynx were also involved. This tumor extended into the esophagus.

LABORATORY FINDINGS

The routine laboratory studies were not reported in this series. The microscopic analyses of one biopsy and two surgical specimens were not recorded. Trible [2] indicated that a roentgenogram of his patient's neck showed negative results.

TREATMENT

The treatment of the patients in this series varied, depending upon the size and location of the lesion. The two small lesions were surgically excised. One involved the left lateral pharyngeal band and was "peanut-sized." The other involved the right lateral pharyngeal wall in the tonsillar fossa and was "walnut-sized." Each of these tumors was localized and bleeding was not excessive during the operative procedures. The small "pea-sized" lesion on the posterior wall of the hypopharynx was successfullly removed through a laryngeal speculum by surgical diathermy.

Three of the large lesions were treated with radium. Two of these occurred in New and Childrey's [5] series. Details of the technic and dosage were not presented but it is implied that a radium applicator was applied to the surface of each lesion. In addition, radium needles and emanation seeds were also employed. Woodward's [3] patient was treated with radium packs applied to each side of the neck. The patient received a total dose of 16,600 mg. hours in three divided doses during fifteen days. One other large lesion involving the hypopharynx and larynx was treated with injections of sodium morrhuate [4].

A method of treatment was not discussed in the case presented by Hayden and Hagens [8]. Wolfenden [1] elected not to treat his patient. Although the lesion involved the right lateral and posterior walls of the pharynx from the soft palate to the base of the tongue, the patient was asymptomatic. "It was judged expedient from the size and extent of the lesion to leave it untouched."

RESULTS

A follow-up report was recorded concerning only one patient in this series. This report by New and Childrey [5] concerned the treatment of a child with a posterior pharyngeal wall lesion with radium. The patient was reported as being well and free from disease six years and three months following treatment.

CASE REPORT

A twenty-three year old married white woman (P. C.) visited my office on April 26, 1960, for evaluation of dysphagia and dysphonia of nine months' duration.

In July, 1959, this patient first recognized difficulty in swallowing and a change in her voice. At that time these symptoms were not alarming; however, as the months passed the symptoms progressed. During the two months prior to examination, she noticed not infrequent episodes of aspiration of saliva and food associated with

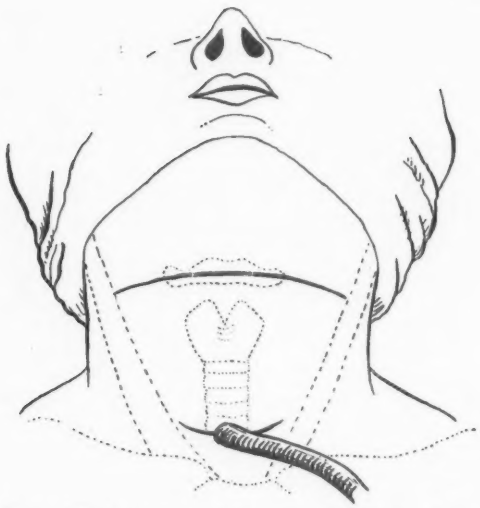

FIG. 1. Tracheostomy and pharyngotomy skin incisions.

FIG. 2. Mobilization of each carotid artery and superior laryngeal nerve.

cough. In addition, her voice gradually assumed a soft nasal quality.

In the spring of 1956, the patient expectorated approximately 4 to 6 ounces of bright, red blood during the course of an upper respiratory infection which persisted for two weeks. At that time she was examined by her family physician. A hemangioma was identified on her posterior oral, pharyngeal wall. On March 3, 1959, she expectorated blood-streaked saliva for a period of twenty-four hours. This occurred at the time of a miscarriage. There was no other history of a bleeding tendency. The past medical history was noncontributory except that her tonsils and adenoids were removed at the age of five years. She is the mother of two normal children, one three years and the other eleven months of age.

Complete examination of this patient showed entirely negative results except for the pharynx. There was identified on its posterior and left lateral walls an elevated, circumscribed, irregular-surfaced, reddish blue, soft, fixed, nonpulsating tumor measuring 8 cm. in its greatest diameter and 2 cm. in its greatest thickness. The pharyngeal mucous membrane covering the superficial surface of the tumor appeared markedly distended and almost transparent. Several 1 to 4 mm., punctuate, grayish red, superficial ulcerations were identified on the surface of the tumor. The tumor extended superiorly to the level of the soft palate and inferiorly to the esophagus. The entire left lateral wall of the pharynx was involved from the upper pole of the posterior tonsillar pillar to the floor of the pyriform sinus. The inferior, posterior and lateral walls of the left pyriform sinus were involved by the tumor. The tumor also involved the posterior wall of the oral and hypopharynges extending to, but not involving, the right lateral pharyngeal wall. The right pyriform sinus was free of disease.

A complete blood count, platelet count, bleeding and coagulation times were within normal limits. A lateral roentgenogram of the soft tissues of the neck confirmed the superior and inferior extent of the lesion. The bony architecture of the cervical spine did not appear abnormal. An esophagram showed negative results.

On May 11, 1960, a tracheostomy was performed under local, Novocaine® anesthesia through a transverse incision at the level of the third tracheal ring. (Fig. 1.) An endotracheal tube was inserted into the trachea through the tracheostomy opening for the administration of oxygen and to maintain an adequate airway during the operative procedure.

Under general anesthesia, a pharyngotomy was performed. (Fig. 1.) A transverse incision was made through the skin and subcutaneous tissues of the neck between the medial borders of each sternomastroid muscle at the level of the hyoid bone. Each external, internal and common carotid artery was mobilized and retracted with umbilical tape loops. The external and internal branch of each superior laryngeal nerve was identified and retracted laterally. (Fig. 2.) The hyoid bone was removed. A transverse incision was made through the vallecula of the tongue from one laryngeal nerve to the other. The base of the tongue was retracted superiorly and the larynx inferiorly. This maneuver gave adequate exposure of the pharynx and the tumor from the level of the soft palate to the esophagus.

The hemangioma was completely removed without difficulty and with minimal loss of blood. There were no large vascular connections extending between the tumor and other vessels of the cervical

spine or neck. The superficial surface of the tumor was covered by pharyngeal mucous membrane and the posterior surface of the tumor rested upon the anterior surface of the cervical spine and the paravertebral muscles. A vertical incision was made through the mucous membrane of the right lateral pharyngeal wall from the superior to the inferior border of the tumor. Parallel, transverse incisions were extended from the superior and inferior extremities of the initial incision to the left and to beyond the left lateral border of the tumor. This rectangular, mucous-membrane flap, hinged at the left lateral pharyngeal wall, was elevated from the superficial surface of the tumor. The posterior surface of the tumor was elevated from the cervical spine and the paravertebral muscles. The entire tumor was excised. (Fig. 3.)

Closure of the pharyngeal defect was accomplished by returning the rectangular, mucous-membrane flap to its original position and approximating its edges to the pharynx.* A feeding tube was passed through the nose and pharynx into the esophagus. The pharyngotomy and skin incisions were closed in layers and a No. 6 tracheostomy tube was inserted into the trachea. The surgical specimen was examined by the pathologist. The gross specimen consisted of a soft, circumscribed, compressible, reddish brown tumor measuring 3 by 2 by 1 cm.

The microscopic description was as follows: "Section through each piece of tissue submitted reveals an essentially similar picture, except that some of the sections do not have a covering, stratified, squamous epithelium. However, for the most part the sections of tissue submitted are covered by a normal-appearing, stratified, squamous epithelium which in some areas is quite flattened, due to a pressure from below by large vascular spaces. The submucous tissue is made up of fibrous tissue infiltrated with a modest number of lymphocytes. Deep to this tissue in two sections, there is a considerable amount of skeletal muscle. The great bulk of the tissue, however, is taken up by vascular spaces that vary in size from simple capillary size to rather large vascular spaces which measure probably up to 0.5 mm. in diameter. These vascular spaces are very irregular and extend throughout the submucous tissue in no definite pattern and extend down into the underlying muscularis. The vascular spaces throughout are lined internally by a flat endothelial surface. Around many of the vascular spaces there is a small component of smooth muscle cells. In some regions this builds into a definite arterial type of vessel. However, for the most part the vascular spaces contain very little or no muscle in their walls. Most of the vascular spaces which are examined contain blood. These findings are consistent with the diagnosis of cavernous hemangioma."

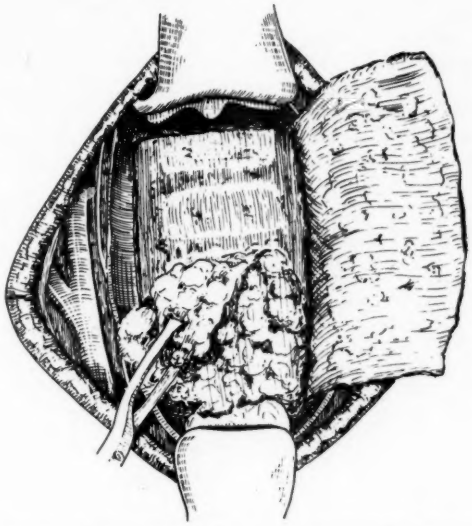

FIG. 3. A rectangular pharyngeal mucous-membrane flap elevated from the surface of the tumor; the tumor excised; flap returned to original position.

The patient's postoperative course was satisfactory even though the rectangular, pharyngeal, mucous membrane flap did not survive. The pharyngeal defect healed by secondary intention. In the immediate postoperative period the patient infrequently aspirated liquids and saliva. She overcame this difficulty and the feeding tube was removed on the fourteenth postoperative day. She was discharged from the hospital on the seventeenth postoperative day. The tracheostomy tube was removed during the fourth postoperative week.

The patient was last examined on October 7, 1960, five months after her operation. There was no evidence of residual disease. The pharyngeal defect had completely healed and the left pyriform sinus was obliterated by scar. Two parallel bands of scar extended between the base of the tongue and the epiglottis on the right. This produced a depression measuring 4 to 5 mm. in its greatest diameter. On occasions debris and food particles collect in this concavity which must be evacuated by manipulation of the tongue. Surgical removal of these bands of scar by direct laryngoscopy is anticipated should the symptoms become more troublesome. The patient is otherwise asymptomatic.

* I am indebted to Leigh K. Haynes, M.D. for his suggestions and association during this part of the surgical procedure.

SUMMARY

Nine cases of cavernous hemangioma of the oral and hypopharynges have been reported

in the English literature since 1887. These cases have been reviewed and analyzed with regard to the age, sex, race, symptoms, duration of the disease, physical signs, laboratory observations, treatment and results of treatment. One additional case of pharyngeal hemangioma has been recorded and discussed.

Acknowledgment: I am indebted to E. Z. Rutkowski for the illustrations.

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Cancer of the Palate

PLASTIC REPAIR VERSUS PROSTHESIS

M. T. EDGERTON, M.D. AND R. V. DEVITO, M.D., *Baltimore, Maryland*

From the Division of Plastic Surgery, Department of Surgery, the Johns Hopkins Hospital and the Johns Hopkins University School of Medicine, Baltimore, Maryland.

IT has been traditional in many medical clinics to repair large palatal defects after surgical removal of cancer of the palate by the use of a dental prosthesis. While undoubtedly of great help, such prostheses have marked limitations. Among these are the problems of oral hygiene, continued difficulty with speech, frequently regurgitation of food or saliva into the nose, and the need to change the size and shape of the prosthesis at reasonable intervals and considerable expense to the patient.

Plastic surgery has been used only infrequently in such instances because of the unfamiliarity of many surgeons with the necessary reconstructive technics, by the fact that usually multiple steps are required to complete the repair, and by the fact that many of the patients requiring this work are elderly. It should be pointed out that only rarely are elderly patients fitted with highly successful prostheses.

We believe that at the present time, physicians are taking insufficient advantage of available surgical methods to offer comfort and happiness to patients with large palatal defects. The repair of the palate with living tissue offers results in terms of comfort, speech, hygiene and eating that are equalled in no other way.

Modern dental prostheses have improved greatly; however, when defects of the palate involve the free border of the soft palate, the prosthesis is faced with the need to create a "seal" in a velopharyngeal aperture that constantly changes in shape with movements of the head and neck. With time, movement of this type also slowly enlarges the anatomic defect. Smaller openings involving only the hard palate are more successfully handled by prosthesis, but these readily respond to simple surgical repair, and in the absence of adequate dentition in the upper jaw, retention of the prosthesis is difficult.

The surgical repair of large palatal defects is dependent on methods to obtain good healing in a kinetic area, bathed in nasal and oral secretions, with gravity acting constantly against the flap tissue in its application against the roof of the mouth. The decision to use surgical reconstruction of the palate thus depends on a safe technic with a high likelihood of success at reasonable cost to the patient in discomfort, time and money.

RESULTS

At the Johns Hopkins Hospital, between 1947 and 1960, 50 patients with major palatal defects were treated by reconstructive surgery. Twenty-seven of these cases were due to loss of the palate following surgery or radiation treatment (or both) for carcinoma. In approximately half these patients the tumor originated in the palate, in the remainder it originated in adjacent structures, primarily the maxillary antrum. Twenty-one patients with congenital defects were treated with extrapalatal tissue repair. Most of these were patients who had had sloughing of palate flaps following improper repair of cleft palatal defects in childhood or infancy.

In seventeen patients with smaller defects, the method of treatment was repair by buccal mucosa or pharyngeal flaps. Thirty-two patients were treated by the use of arm, cervical, chest or forehead flaps.

Eight patients in this group were judged to have had optimal prosthetic replacement by competent prosthodontists. After wearing the

FIG. 1. (JHH # 248976) This patient (R. M.) was first seen with this lesion at the age of fifteen. A well encapsulated mixed tumor of the cylindroma type was excised with adequate microscopically verified margins using electrocautery. At twenty-two years of age she required left radical neck dissection and at twenty-five died of the metastatic disease. Such tumors must be treated as malignancies.

prosthesis for several years they then were subjected to surgical repair and in *every* instance stated that the surgical closure was much more satisfactory in terms of "comfort," "cleanliness" and "sense of deformity."

METHOD OF PLASTIC REPAIR

The method of reconstruction, of course, depends upon the size of the defect and the time at which the opportunity for reconstruction is presented. For smaller defects, usually local flaps of palatal or buccal mucosa can be transferred in the manner described by Cupar [2], Padgett [6] and others [5]. However, it should be stressed that the surgeon who removes the initial tumor often has the only opportunity to utilize immediate reconstruction in a way that may save the patient much larger and more complicated operations later [4]. This is particularly true in two circumstances, the first of which is when a low grade malignant tumor, such as the mixed tumor or adenocarcinoma of the palate, requires removal of oral mucosa and bony palate, but permits preservation of the nasal mucous membrane. (Figs. 1 and 2.) In this circumstance the immediate application of a split-thickness graft to the delicate nasal mucosa will permit immediate one stage repair and will hinder in no way subsequent follow-up treatment for

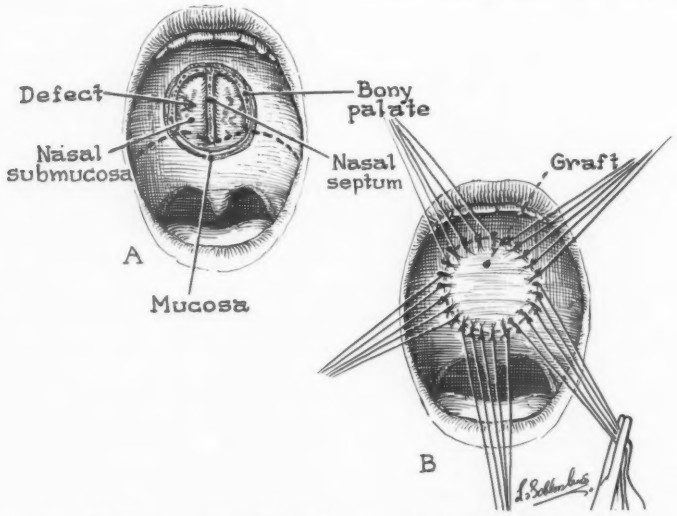

FIG. 2. This illustrates the type of defect (A) which is produced by adequate excision of mixed tumors of the palate; the nasal mucosa is left intact to receive a split-thickness skin graft which is held in place by a "tie-on" dressing (B).

tumor recurrence. If this is not performed *immediately*, the thin nasal mucosa will not survive and a full-thickness defect often results.

The second group of smaller lesions permitting immediate reconstruction are those involving the free border of the soft palate; in these, the immediate use of a posterior pharyngeal flap will leave the patient with almost no speech impairment. The prosthetic replacement of tissue in this region of the palate has proved most satisfactory in similar cases. The length of the flap should be adequate to allow for some shrinkage and the width of the flap should be approximately three-quarters the total width of the nasopharynx. Such a pharyngeal flap can also be used as a secondary procedure to restore velopharyngeal competency when portions of the soft palate have been resected in major removal of the tonsil or base of the tongue for carcinoma.

Healed fistulas in the region of the hard palate may be handled by a variety of reconstructive technics [*1,4,5*]. In general, the principle involves the formation of a double-layered closure consisting of "turn-in" flaps of palatal tissue to line the floor of the nose, covered by shifted or rotated flaps from the buccal mucosa or palate to supply epithelial lining on the oral surface of the defect. In some instances "delays" of the lining or oral flaps may be required before actual transfer.

Larger palatal fistulas in our experience have been more commonly neglected by surgeons. They are generally secondary to resections for advanced carcinoma and should not be reconstructed until the surgeon is reasonably sure there will be no recurrence, *or that there can be no further reasonable local excision even if recurrence develops*. If there is doubt about the need for further excisional surgery, a prosthetic obturator should probably be used until that doubt is resolved. It should be stressed that it is of great help to the reconstructive surgeon (in patients in whom these problems are expected) if preoperative dental impressions are taken and the existing teeth to be retained are properly prepared for prosthetic fitting. If reconstruction requires the use of pedicle flap tissue from an extraoral location, it should probably not be undertaken unless the operator has had considerable experience with the migration of pedicle flaps. If he has this experience, we are convinced that a uniformly high percentage of good results may be obtained. We do not believe the traditional use of the arm flap [*5*] is warranted, as it presents technical problems to the surgeon and the patient that are readily avoided by the use of cervical tubes or [*4*] forehead flaps.

Our preference for closure of these defects is a generous cervical tube, raised horizontally on the neck and later passed through the mouth on the deep surface of the mandible. The tube should be placed low on the neck and planned so that it will have adequate length to permit gentle curving without tension. The donor site can almost always be closed primarily by undermining. After three weeks the distal end of the tube is appropriately delayed. This has the advantage of producing an additional layer of collagen which stiffens that portion of the tube to be used to replace the bony palate. After a further two weeks the flap is transferred through the floor of the mouth and sutured into the defect. (Fig. 3.) Earlier methods in which tubes were transferred to the palate through the oral stoma should be avoided. Admitting the flap to the palate through the mouth interferes with operative visibility and postoperative feeding. It results in a dry mouth and considerable efforts are required to avoid having the patient bite down on the tube during sleep.

Postoperatively, general dilatation of the passageway through the floor of the mouth may be required, but there is generally no leakage of saliva onto the neck.

A lining flap to the floor of the nose must be provided in all large palatal defects. This may be obtained by a "turn-in" flap from the edge of the defect or by use of the tube itself. It is extremely important that the flap be supported in the postoperative period to overcome the effects of gravity and prevent motion by movements of the tongue. (Fig. 3.) We generally create a simple crossing of steel wires to form a support for light packing between these wires and the implanted flap. The packing is removed and the suture lines are inspected and cleansed daily.

If the palatal defect is part of a maxillectomy defect, the denuded dermal-fatty core of the tube can be implanted into the subcutaneous tissues of the cheek to improve contour. We have found the use of the cervical tube flap to be greatly superior to that obtained from the inner aspect of the upper arm, the shoulder, the abdomen or the thorax.

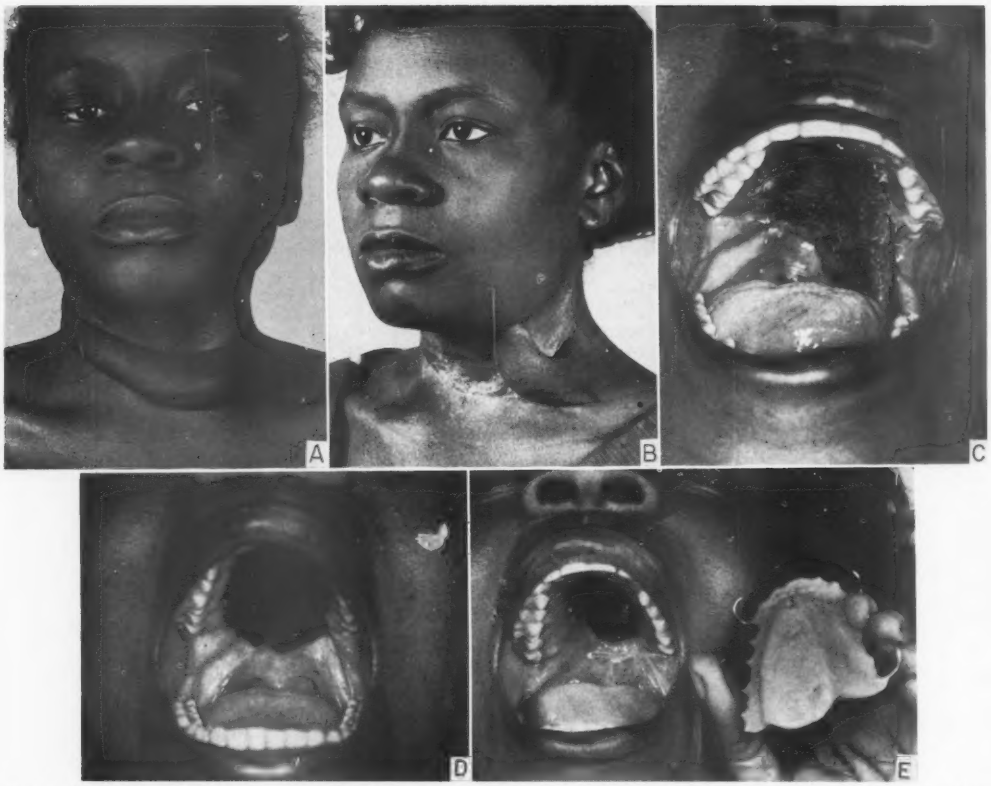

FIG. 3. (JHH # 423980) During a pregnancy at the age of twenty-two, a rapidly growing tumor of the hard palate developed in this patient (D. F.). This proved on biopsy to be a squamous cell carcinoma. On June 23, 1954, wide excision to include the left hard palate, the vomer and inferior septum, inferior turbinate on the left, and a portion of the soft palate was performed. She wore a prosthesis temporarily (E) but was unhappy with her "cleft palate" speech and with nasal escape of fluid and food particles. Reconstruction was begun on April 7, 1955, with formation of a cervical tube (A). After split-thickness lining of the distal paddle, the tube was carried through the floor of the mouth and into the defect on July 27 (B and C). The pedicle was divided and the graft tailored into place on September 12 with the final result shown in D as compared to her previous status in E. The patient continues to be well and satisfied.

PALATAL AND FACIAL DEFECTS

The combined defects of the palate and cheek are usually secondary to radical maxillectomy requiring exenteration of the orbit and sacrifice of overlying involved soft tissues. This produces a massive defect, but it is now possible even in the elderly patient to repair satisfactorily the function and appearance of these patients. Formerly, we believed that obliteration of the facial defect was the major surgical need and tended to rely on a prosthesis for the large palatal defect [9]. With increasing experience we have come to believe that the most important need for living tissue in these patients is the establishment of an intact and functioning palate that greatly improves breathing, speech and feeding and that this should precede obliteration of the orbital or facial defect. It should be pointed out that repair of the palate usually does not interfere in any way with follow-up treatment of the cancer.

Our experience with the use of split-thickness grafts from the lower neck and upper chest to the face [3] has been so gratifying in terms of color match, that without hesitation we now utilize the full width and height of the forehead as an immediate undelayed, readily available pedicle flap for these large facial and palatal

FIG. 4. (JHH # 744631) This fifty-one year old man (F. M.) when first seen on October 30, 1958, had a massive squamous cell carcinoma of the left antrum which was breaking through the hard palate (A). Following a therapeutic course of 4,500 r through two left and one right maxillary ports, radical excision was undertaken on January 8, 1959, producing the defect seen in B. A further course of 5,000 r was given postoperatively to the ethmoid and pterygoid areas. Reconstruction was begun on December 16, 1959, with elevation and lining of a forehead flap (B). This flap was rotated into the palate on January 23, 1960, and the donor site split grafted (C). The status following this procedure is shown in D; subsequently, complete obliteration of the orbit was accomplished with the remaining forehead flap.

defects. The typical defect consists of a large ovoid, split graft lined cavity extending from the lateral border of the nose to the zygomatic arch and from the eyebrow to the upper lip at the alar level. This cavity looks down onto the tongue, since the alveolar ridge and most of the palate have been removed. (Fig. 4.)

The stages in reconstruction utilizing the forehead flap are as follows:

1. At tumor resection, a bipedicle flap of the forehead is elevated down to the periosteum from ear to ear and hairline to browline with both temporal arteries left intact. The flap is lined with a split-thickness skin graft on its

under surface and is sutured back into place.

2. Ten days later the contralateral temporal pedicle is divided horizontally on a line with the outer canthus of the eye. The lined flap is elevated and the distal end is transferred into the palatal defect through the facial opening and placed so that the forehead skin is directed orally. The skin graft lining thus furnishes the new nasal floor. The margins of the defect are prepared by elevation of narrow flaps of mucosa and skin graft to furnish a better base for attachment. Thus, at one stage the entire palatal defect is closed with the distal part of the lined forehead flap. The granulating forehead defect is then grafted with a large split-thickness graft taken from the lower neck or upper chest [5]. It is essential to support and immobilize the palatal portion of the flap as much as possible. This is done by using gavage feeding, and discouraging talking or swallowing, and by supporting the flap with an oral "wire-basket" arrangement over packing.

3. In three to five weeks the flap circulation is usually adequate at the implanted end, the proximal forehead pedicle is divided and the remaining flap used for partial or complete obliteration of the orbital and cheek defect. We sometimes leave a temporary opening between the edge of the flap and the side of the nose to aid with irrigation of the cavity or follow-up examination for tumor until satisfied with the patient's progress. At that time, with the patient under local anesthesia, the flap can be simply opened at the folded margin and sutured to the nose. (Fig. 4.)

Thus, the entire palatal-facial reconstruction required only one additional operation and three weeks in time over simple obliteration of the cheek defect. It should be noted that the magnitude of the palatal defects in these patients usually prevents retention of any ordinary palatal prosthesis.

SUMMARY

We have become increasingly convinced at Johns Hopkins Hospital that surgical repair of large palatal defects is warranted in the vast majority of instances. The impetus for repair has come to us from patients who have been unhappy with prostheses. The sophistication of general surgical and plastic training has produced an adequate number of surgeons now trained to perform not only extirpation but the equally important reconstruction of the resulting defects.

Reconstruction should always be planned and often initiated at the time of original resection of palatal tumors. Of course, highly suspicious margins should not be hidden from view until they are shown to be tumor free clinically and on biopsy. Small palatal defects may close spontaneously. Moderately sized ones may require local oral tissue repair. With larger defects the cervical and forehead tissues are the prime donor sites for flap migration. They permit rapid transfer with minimal deformity, cost and inconvenience to the patient. We prefer not to pass such flaps through the mouth to reach the palate, but prefer access by means of an existing orbital or facial defect, or by incision through the floor of the mouth.

Surgeons are urged to think more often of immediate split grafting of the nasal mucosa and the immediate use of pharyngeal flaps with removal of smaller tumors from the palate.

Our experience with this group of patients has demonstrated that the use of autogenous living tissue for the repair of acquired defects of the palate offers many advantages that have long been recognized in the surgery of congenital clefts.

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Bilateral Radical Neck Dissection Performed in Stages

EXPERIENCE WITH 467 PATIENTS

EDGAR L. FRAZELL, M.D. AND OLIVER S. MOORE, M.D., *New York, New York*

From the Head and Neck Service of the Memorial and James Ewing Hospitals, New York, New York.

BILATERAL cervical lymph node metastasis is a significant feature in the clinical course of numerous patients with cancer of the head and neck region. Such spread may be evident on initial examination in some; while in others, metastasis to one side of the neck may antedate discovery of involvement of the second side by weeks, months or even years. In any case "when a patient presents himself with cervical metastasis, or if metastasis develops in a contralateral neck subsequent to a neck dissection, the prognosis is grave but not necessarily hopeless" [*1*].

Medical literature contains relatively few references to bilateral radical neck dissections. It is evident that surgeons have been slow to propose that the standard operation, including resection of the internal jugular vein, be performed bilaterally for fear that obstruction to venous return might cause dangerous increase in the intracranial pressure. Examination of the records of patients treated at the Head and Neck Service of Memorial Hospital indicates that until relatively recent times, i.e., approximately twenty-five years ago, members of our staff shared this opinion. When confronted with the development of metastatic cancer in the second side of the neck in a patient previously treated by radical neck dissection, surgeons were prone either to advise radiation therapy or to be content with an incomplete operation.

Priority in confirming the fact that both internal jugular veins in man could be excised in stages without causing serious or lasting sequelae has not been established. In our clinic, it is apparent that sacrifice of the second internal jugular vein was initially undertaken with considerable trepidation [*2*]. The lack of serious complications in our first patient, and the fact that she apparently remained free of disease, was greeted with considerable enthusiasm and encouraged further curative efforts with this method. At the present time, in this clinic, surgeons regularly employ bilateral neck dissection, when indicated, in the treatment of patients with cancer of the head and neck region.

It is the purpose of this report to record our experience with patients treated in this manner.

MATERIALS AND METHODS

During the twenty year period (1940 to 1959) covered by this report, bilateral radical neck dissection performed in stages was an integral part of the treatment for cancer in 467 patients in this clinic. In one patient, initial neck dissection was performed by us in 1939; and in three patients, it was performed in other hospitals prior to referral of the patient to us. In all other patients both sides of the neck were dissected by members of our staff during the period under review. The operation on each side consisted of the standard radical dissection, and thus both internal jugular veins were excised in each patient.

The distribution of patients by the year when the second side of the neck was dissected (Fig. 1) indicates the increasing frequency with which this method of treatment has been employed in this clinic.

Age and Sex. The age of patients at the time of the second neck dissection varied from youth to advanced age. Our youngest patient was a four year old girl who had extensive bilateral cervical metastasis from cancer of the thyroid.

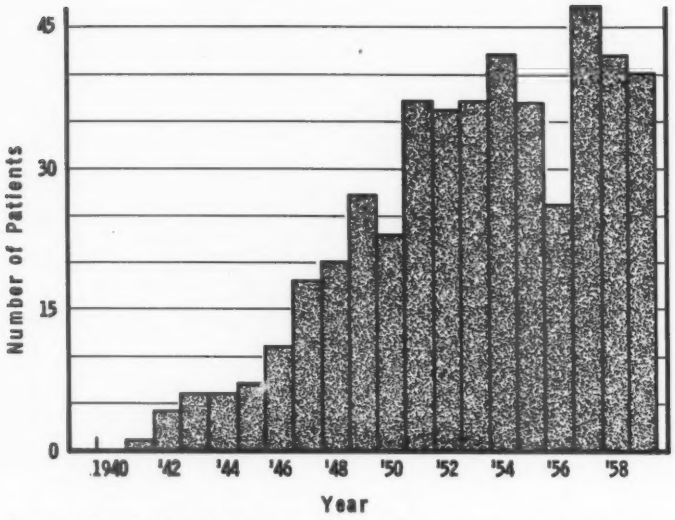

FIG. 1. Distribution of 467 patients according to the year of the second neck dissection.

The oldest patient was an eighty-five year old man whose primary lesion was cancer of the floor of the mouth. The median age of patients in this series was fifty-seven years. Men comprised 81 per cent of the group.

Primary Lesion. Patients treated by bilateral neck dissection included those with a wide variety of primary lesions. In all except three patients, the primary lesions were located in the head and neck region. One patient had cancer of the breast that metastasized to each side of the neck without other evidence of disease. In two patients, the primary lesion was occult but was thought to be located in the nasopharynx. The distribution of patients according to the site of the primary lesion (Table 1) not only reflects the relative incidence of such growths in patients treated in this clinic but is also indicative of the relative frequency of the tendency to spread bilaterally.

The primary lesion in some patients in this series was healed as a result of previous therapy. In others, the size varied from minute lesions, often accidentally discovered, to growths of extreme bulk. The relationship between the size of the primary lesion and the tendency to bilateral cervical metastasis is not constant. However, in this series, the primary lesion in

TABLE I
SITE OF PRIMARY LESION ON ADMISSION

Site	No. of Patients
Tongue	121
Extrinsic larynx	82
Floor of mouth	57
Thyroid	47
Intrinsic larynx	27
Gingiva	26
Tonsil	22
Lip	17
Soft palate	15
Nasopharynx	15
Pharyngeal wall	12
Miscellaneous*	26

* Skin, nine; buccal mucosa, five; hard palate, three; paranasal sinuses, three; major salivary glands, three; breast, one; unknown, two.

TABLE II
CERVICAL METASTASIS ON ADMISSION

Location	No. of Patients	Per cent
Neck clinically normal (primary cases)	148	32
Neck clinically negative (previous treatment)	66	14
Metastasis on one side	211	45
Bilateral metastasis	42	9
Total	467	100

TABLE III
INITIAL TREATMENT AT MEMORIAL HOSPITAL

Treatment	No.
Primary lesion	
Surgical excision	411
Radiation	42
Primary not treated*	14
	467
Cervical metastasis	
Neck dissection and primary excision (combined operation)	326
Neck dissection and primary excision (separate operations)	6
Neck dissection only	135
Total	467

* Previous treatment successful in twelve, primary occult two.

one-half the patients was estimated to be 3 cm. or more in diameter, and in this group of bulky tumors, the incidence of invasion of adjacent structures was high.

Cervical Metastasis. Not all patients treated with bilateral neck dissection had clinical evidence of metastasis at the time of admission, (Table II), and some of them lacked clinical evidence of cervical metastasis at the time of the initial neck dissection. In the latter category were patients whose neck appeared clinically negative for abnormalities after local excision of nodes prior to admission to this clinic. Patients with extensive cancers that invaded adjacent structures often underwent routine neck dissections as part of a combined operation even though there was no evidence of cervical metastasis. Regardless of the findings in the neck at the initial dissection, metastasis to the second side of the neck was invariably suspected in all patients prior to the second neck dissection.

MEMORIAL HOSPITAL TREATMENT AND CLINICAL COURSE

Primary Lesion. The overwhelming majority of patients in this series underwent surgical excision as the initial treatment of the primary lesion. (Table III.) This is in keeping with the policy of the Head and Neck Service of the Memorial Hospital.

Previous treatment of the primary lesion had been successful in twelve patients who required no further treatment for disease at that site. The primary lesion was never discovered in two patients. One of them died of disseminated cancer one and a half years after the second neck dissection and one patient is alive and well seven years after the first neck dissection and five years after the second. (Fig. 2.) The radical combined operation of excision of the primary lesion plus neck dissection was employed as the initial treatment in three fourths of the patients in this series.

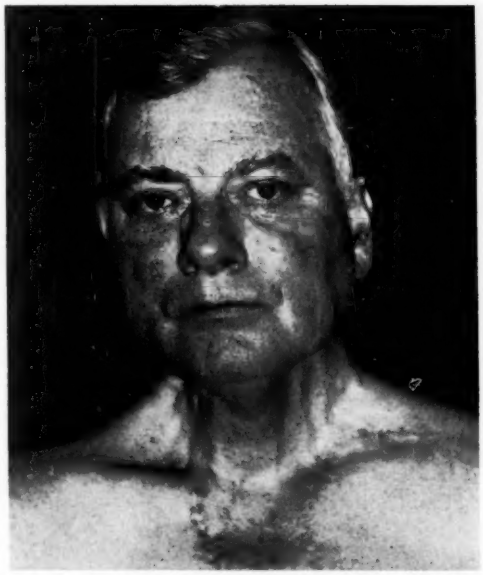

FIG. 2. Appearance of patient seven years after the first neck dissection and five years after the second neck dissection for metastatic cancer from an unknown primary site. Note the lack of significant edema.

Interval Between Operations. During the early years of this experience, patients were not considered suitable for bilateral neck dissection unless the operations could be spaced several months apart. Generally speaking, it was thought that the longer the interval between operations, the less likelihood of undesirable sequelae. Experience failed to confirm this belief and the permissible interval was gradually shortened. This was fortunate since the majority of patients showing bilateral cervical metastasis do so fairly early in the clinical course. Thus, one-half the patients undergoing bilateral neck dissections had both operations within six months of admission and three-fourths of them within the first year.

TABLE IV
INTERVAL BETWEEN NECK DISSECTIONS

Interval (mo.)	No. of Patients
Less than 1	43
1 to 3	118
4 to 6	97
7 to 12	94
More than 1 yr.	115
Total	467

TABLE V
SURGICAL COMPLICATIONS IN 141 PATIENTS*

Complication	No. of Patients
Wound infection and slough	84
Persistent facial edema	28
Pharyngeal fistula	24
Cerebrovascular accident	4
Chyle fistula	7
Respiratory obstruction	6
Major hemorrhage	4
Shock and hypotension	10
Hypoparathyroidism	6
Cardiac arrest	3
Postoperative death	8
Total	184

* Complications were multiple in some patients.

(Table IV.) The shortest interval between neck dissections was seven days, and the longest was over ten years. Among the patients who had the neck dissections spaced more than one year apart were eleven who had the second operation five to ten years after the initial dissection and three who had the operations ten or more years apart. There were fifty-four patients who had the second neck dissection associated with reactivity of disease at the primary site. Ten patients underwent a second neck dissection as part of the surgical treatment of a new primary lesion.

Complications. Complications of a more or less serious nature were observed in approximately 30 per cent of the patients after the second neck dissection. (Table V.) The most frequent complications recorded were associated with faulty wound healing characterized by infection and slough of skin flaps. Such complications were most frequent in patients in whom the second neck dissection was combined with other resections such as those for a new primary lesion or recurrence at the site of the primary. Under such circumstances the complications were frequently multiple and included pharyngeal fistulas, hemorrhage and the like.

Following bilateral neck dissection, most patients exhibit some degree of facial edema. In the majority, this is transient, minimal and differs little from that observed following a single neck dissection. In others, it is of greater degree, persists for weeks or months, and leaves residual thickening in the parotid and submaxillary areas. Finally, in a few patients the edema is marked and permanent, and results in a grotesque facial appearance.

In its onset, facial edema that follows a second neck dissection may be abrupt or gradual in onset. If abrupt, this is noted shortly after ligation of the internal jugular vein and is characterized by massive swelling of the eyelids, tongue and glottis, and, when accompanied by cyanosis, erroneously gives cause for alarm. In such patients, obstruction of venous return appears to be the causative factor in the signs observed. Fortunately, such sequelae are usually transient and in no instance have they been associated with the death of the patient. In the majority of patients in whom postoperative edema develops, the onset is gradual and reaches its peak seven to ten days after surgery. The degree of edema is variable and is rarely accompanied by cyanosis. Lymph stasis rather than venous obstruction appears to be the source of this complication. There appears to be no relationship between the degree of postoperative edema and the interval between operations in patients treated by bilateral neck dissection.

There were eight postoperative deaths (1.7 per cent) following bilateral radical neck dissection and, as previously noted, none of these could be attributed to the sacrifice of the second internal jugular vein. This record compares favorably with that achieved following unilateral neck dissection.

Other postoperative complications noted following bilateral neck dissection differed little from those observed following single neck dissection.

Duration of Hospital Stay. Patients who underwent bilateral neck dissection were rarely hospitalized for a longer period of time after

TABLE VI
DURATION HOSPITAL STAY

Duration (wk.)	No. of Patients
Less than 2	323
2 to 3	81
3 to 4	40
Longer than 4	23
Total	467

the second operation than they were after the first operation. This is of interest in view of the high incidence of reportable complications. In 323 patients (70 per cent), the duration of hospital stay was less than two weeks (Table VI) and in 95 per cent the stay was less than four weeks. Patients requiring prolonged hospitalization were usually those who had the second neck dissection in combination with resection of other structures when, as previously noted, the incidence of severe complications was high.

Multiple Primary Lesions. Numerous observers have recorded the occurrence of multiple primary cancers in the same patient. Experience in this clinic suggests that this incidence (omitting skin cancer) approaches 10 per cent and seems greater than can be accounted for by chance alone. In this series of patients who had bilateral neck dissections, in forty-two (8.9 per cent) more than one primary cancer developed during the period of observation. Although the records indicate that in only ten patients was the treatment of the second cancer associated with the second neck dissection, all but four of the second primary lesions were located in the head and neck region. (Table VII.)

TABLE VII
MULTIPLE PRIMARY CANCERS

Site of Second Cancer	No. of Patients
Extrinsic larynx	7
Tongue	6
Thyroid	4
Soft palate	4
Floor of the mouth	3
Gum	3
Tonsil	2
Skin	2
Pharyngeal wall	2
Buccal mucosa	2
Intrinsic larynx	1
Nasopharynx	1
Cervical esophagus	1
Other*	4
Total	42

* Lung, two; stomach, one; bladder, one.

LABORATORY FINDINGS

Primary Lesion. Histologic proof of a primary cancer arising in the head and neck region was available for all but the three patients previously noted. Eighty-five per cent of the tumors were epidermoid or squamous carcinoma. The remainder were adenocarcinomas arising in the thyroid or in the major or minor salivary glands. Thyroid adenocarcinomas were four times as frequent as were other adenocarcinomas. The latter, for the most part, arose in the minute mucous glands of the palate, tongue, etc.

Cervical Nodes. Laboratory examination of the specimens of neck dissection revealed that 375 patients (80.3 per cent) had metastatic nodes bilaterally. Metastatic nodes were found on one side of the neck only in eighty-three patients (17.7 per cent) while in nine patients there was no laboratory evidence of lymph node metastasis in either side of the neck. The

TABLE VIII
STATUS AT FIVE YEARS IN PATIENTS TREATED BY BILATERAL RADICAL NECK DISSECTION

Site of Primary Cancer	No. of Patients	Living Free of Cancer	
		No. of Patients	Per cent
Tongue	78	18	23
Extrinsic larynx	53	11	21
Floor of mouth	39	4	10
Thyroid	38	32	84
Intrinsic larynx	19	3	11
Gingiva	20	4	20
Tonsil	12	1	8
Lip	14	5	36
Soft palate	12	3	25
Nasopharynx	4	1	25
Pharyngeal wall	5	1	20
Miscellaneous	18	6	33
Total	312	89	29

relationship between these laboratory findings and the end results of treatment is of considerable interest.

COMMENTS

The tendency of primary cancer of the head and neck region to remain localized to the primary site and regional lymphatics for prolonged periods of time is well known. It is evident that extensive and often bilateral involvement of cervical lymph nodes often precedes dissemination to distant sites. This fact makes attempts at surgical cure by neck dissection reasonable as long as the primary focus of the disease is under control or is controllable. Bilateral neck dissection is not inconsistent with this objective and, as is shown (Table VIII), is successful in a gratifying number of patients.

Of the 467 patients treated by bilateral radical neck dissection during the period under review, 312 (66.8 per cent) were available for five year end result analysis. There were eighty-nine patients (28.5 per cent) who were living and free of cancer five years after the second neck dissection. This is considered outstanding in view of the finding that three-fourths (74.1 per cent) of the survivors had laboratory confirmation of bilateral lymph node metastasis of the neck. An additional 22.5 per cent of the survivors had metastasis to one side of the neck only.

The percentage of five year cures varied widely according to the location of the primary lesion. Patients treated by bilateral neck dissection were a highly selected group, and the results achieved did not, in general, reflect the relative curability of cancer arising in various anatomic sites. It is of interest to note that cancer of the lip proves to be a highly lethal disease once metastasis to one or both sides of the neck has occurred. The results obtained in cancer of the intrinsic larynx were particularly disappointing and, when compared with cancer of the extrinsic larynx, are not readily explained except on the basis of difference in the size of samples. Results for patients with bilateral metastasis from cancer of the soft palate, gingiva, nasopharynx and pharyngeal wall were encouraging when treated by bilateral neck dissection. Patients with bilateral cervical metastasis from cancer of the thyroid had tumors that were mostly papillary in type and the end results reported differed little from those usually reported in the literature.

The results of this experience should encourage surgeons engaged in the treatment of cancer of the head and neck region.

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A Muscle Cover for the Carotid Artery After Radical Neck Dissection

CHARLES J. STALEY, M.D., *Chicago, Illinois*

From the Departments of Surgery, Veterans Administration Research Hospital and Northwestern University Medical School, Chicago, Illinois.

MARGINAL NECROSIS of the skin flaps is an occasional sequel of extensive surgical procedures in the cervical region. Here, even minimal slough of skin may be a serious complication, for with the conventional incision the cutaneous defect is always adjacent to the carotid artery. The artery, thus deprived of its only protective cover, may undergo necrosis, particularly when associated with a pharyngocutaneous fistula; severe hemorrhage follows. Death may occur before bleeding can be controlled. It may also occur as a consequence of carotid ligation. Although carotid ligation is mandatory, the surgeon's apprehension is not completely relieved despite the fact that the majority of patients tolerate ligation with little difficulty. Even prophylactic ligation of an exposed but intact carotid artery is not ordinarily undertaken without thoughtful hesitation.

Significant loss of skin flaps is an unusual occurrence after a conventional radical neck dissection but it is not unusual when dissection is accomplished after previous radiation. It also may follow bilateral radical neck dissection and neck dissections performed in continuity with laryngectomy or thyroidectomy. Less often, radiation necrosis occurs long after neck dissection has been accomplished.

An analogous problem may confront the surgeon following ilioinguinal lymph node dissection, for healing is notoriously poor after this operation. In fact, primary healing in a literal sense is unusual. Exposure of the femoral vessels may result from necrosis of the subinguinal portion of the flaps but can be prevented by transplanting the upper end of the sartorious muscle over the femoral triangle. This technical maneuver, described by Baronofsky who attributed its conception to Wangensteen, has attained wide acceptance. The levator scapulae muscle may be used in similar fashion to provide additional protection for the carotid artery following radical neck dissection.

Within recent years, many incisions which differ markedly from the conventional T, Y, and double-Y, have been recommended. The proponents of these incisions emphasize that healing and cosmetic result are improved. A modest personal experience with such incisions would tend to confirm these observations. Nevertheless, the absence of necrosis of skin flaps does not necessarily assure the integrity of the carotid artery, for the fistula which occasionally follows incontinuity excision of the mandible, oropharyngeal structures or larynx may place this vessel in jeopardy.

TECHNIC

The levator scapulae muscle arises by tendinous slips from the transverse processes of the first four cervical vertebrae. It inserts into the vertebral margin of the scapula from the upper angle to the spine. The anatomy of the muscle is inconstant, the number of vertebral attachments may vary, a slip of muscle may extend to adjacent bony or muscular structures or it may be divided throughout much of its length. The muscle raises the scapula and draws it medially. When the scapula is fixed, it bends the neck laterally and rotates it toward the same side.

The levator scapulae muscle receives its innervation from the anterior primary rami of the third and fourth cervical nerves. There is often an additional branch from the dorsal scapular nerve which is derived from the fifth cervical nerve. Blood is supplied by branches of the descending portion of the transverse

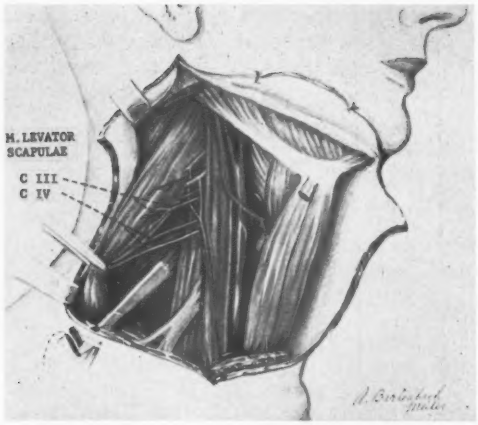

FIG. 1. The levator scapulae muscle is divided at its scapular insertion.

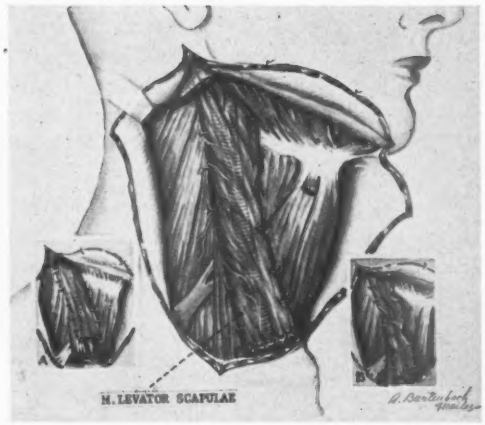

FIG. 2. The muscle is rotated 180 degrees and sutured, to the stump of the sternomastoid muscle; inset A, lower portion of carotid artery remains uncovered due to debridement of lower end of muscle; inset B, muscle lengthened by transverse step-ladder incisions.

cervical artery, the occipital artery, and other small unnamed vessels. It is important to note that the vessels and nerves enter the anteromedial aspect of the muscle and limit the range through which it may be displaced. *The blood supply of the muscle may be compromised if mobilization is not cautiously performed.*

The cervical portion of the muscle is exposed during the dissection of the posterior triangle; the remaining segment is readily traced to its scapular insertion. The fascia at the anterior and posterior edges of the muscle is incised, the distal portion of the muscle is elevated and the scapular attachment transected. (Fig. 1.) Mobilization is accomplished without difficulty and without extension of the incision. The posterior edge of the muscle is mobilized to its origin from the transverse processes of the upper cervical vertebrae. The lower portion of the anterior edge of the muscle is completely freed but care must be exercised in order to preserve the blood supply. The lower end is then displaced anteriorly and sutured to the clavicular stump of the sternomastoid muscle. Since the nerves and vessels enter at the anterior margin, it is usually impossible to displace the muscle sufficiently unless it is rotated 180 degrees in its long axis. The muscle is turned on itself, from behind forward, like turning the page of a book; the posterior margin then becomes the anterior margin. Anteriorly, the muscle is sutured to the strap muscles if they remain in the operative field, or to the prevertebral fascia if laryngectomy or thyroidectomy has been accomplished. The edge of the levator scapulae is sutured to the digastric muscle superiorly and to the prevertebral fascia overlying the scalene muscle posteriorly. (Fig. 2.) Care is taken to avoid the phrenic nerve. A muscular sheath which covers the carotid vessels throughout their course in the cervical region is thus created. The vessels not only are protected should there be a slough of the overlying skin but also are protected if an oral or pharyngeal fistula develops.

When this maneuver was initially utilized, the muscle was mobilized after the operation was otherwise completed, i.e., immediately prior to the closure of the skin. But in one instance, perhaps two, the lower end of the muscle subsequently became necrotic. We now elevate the muscle earlier in the operation so that any devitalized tissue might become manifest before the wound is closed. Should the lower end of the muscle appear nonviable, it is trimmed away until bleeding occurs. If the muscle is unduly shortened by this debridement, small transverse step-ladder incisions may be made along either edge (after the fashion of tendon-lengthening procedures) to provide additional length. If this does not provide sufficient tissue, the lower end of the carotid artery may be covered by reflecting the sternothyroid muscle laterally. Complete coverage of the artery may be unnecessary, for in the vast majority of patients it is the

area at or near the level of the carotid bulb which is exposed. Covering the upper portion of the artery may be as effective as covering the entire vessel.

INDICATIONS

It is not our belief that transplantation of the levator scapulae muscle is necessary after all radical neck dissections, but we consider it especially advantageous under certain circumstances. Previous radiation of the cervical region increases the likelihood of inadequate healing after neck dissection alone or incontinuity with resection of the primary tumor. And marginal necrosis of the skin flaps follows one stage bilateral neck dissection, and neck dissection in continuity with thyroidectomy, laryngectomy and laryngopharyngectomy, with sufficient frequency that this precautionary measure seems desirable. Fistula formation is not rare after the latter operations. Transplantation of the levator muscle is also indicated when a strategic cutaneous defect exists following the excision of a primary epidermoid carcinoma or melanoma of the cervical skin or the removal of nodes that have secondarily involved this skin.

This maneuver was initially planned with the hope of eliminating hemorrhage after neck dissection but additional assets may be noted. The transplanted muscle minimizes the flattening occasioned by the removal of the sternomastoid muscle. It also eliminates the prominence produced by the pulsating carotid bulb which is sometimes disturbingly visible to the patient. In addition, the muscle mass partially eliminates the dead space in the supraclavicular fossa.

COMPLICATIONS

The majority of individuals who have undergone a radical neck dissection have some complaint referable to the shoulder. Our limited experience suggests that the early postoperative discomfort may be aggravated by levator transplantation but the discomfort has not been distressingly severe nor has it persisted in the late postoperative period. Gross clinical measurement has not demonstrated a greater functional disability than that which accompanies the conventional dissection. More refined studies are in progress. It is likely that other muscles of the shoulder girdle adequately compensate for the functional loss of the relatively unimportant levator scapulae muscle.

The only significant complication that we have noted resulted from the devitalization of the lower end of this muscle. We are certain that some necrosis occurred on one occasion and suspect it may have occurred on another. It is hoped that elevation of the muscle early in the procedure, with debridement before transplantation when necessary, will eliminate this complication.

It is with some misgiving that we mention the occurrence of massive hemorrhage in one patient, following partial glossectomy and mandibulectomy, laryngectomy and bilateral radical neck dissection for multiple primary tumors with bilateral metastases. A large pharyngeal fistula developed and was followed by an extensive slough of the skin flaps. Covering the upper portion of the left carotid artery had been difficult and it was from this point that hemorrhage occurred. The muscle had retracted, permitting exposure of the vessel. A skin slough of equal magnitude occurred on the opposite side but the right carotid artery was not exposed. Rotating the muscle in its long axis, as is now done, would have prevented this mishap. We consider this a failure of application of the method rather than a failure of the method *per se*.

SUMMARY

A modification of the conventional radical neck dissection is described in which the levator scapulae muscle is transplanted to provide a protective sheath for the carotid artery. It is hoped that this maneuver will eliminate the occasional hemorrhage which follows extensive surgery in the neck. It has been accomplished in only twelve instances and is not considered a procedure of established value. Additional experience is needed before final evaluation can be made.

Results of Cytologic Studies of Wound Washings and Use of a Local Cytotoxic Agent in Head and Neck Surgery

KUMAO SAKO, M.D., FRANK C. MARCHETTA, M.D., JORGE BADILLO, M.D. AND EUGENE BURKE, B.S.,
Buffalo, New York

From the Departments of Surgery and Pathology, Roswell Park Memorial Institute, Buffalo, New York.

THE APPEARANCE of local recurrent lesions in the head and neck region following wide radical surgery has been a source of keen disappointment to us, particularly after a seemingly adequate resection as evidenced by careful pathologic examination of resected borders and sections of three different levels of each node in cleared specimens.

The appearance of multifocal lesions (Fig. 1) has suggested to us and to other observers that these recurrences were possibly due to seeding of the wound by cancer cells at time of surgery. In the recent literature, numerous investigations have dealt with the occurrence of tumor cells in wound washings [*1–3*], and with the use, both experimental and clinical, of topical chemotherapeutic agents for irrigation of wounds [*4–10*].

FIG. 1. Multiple foci of local recurrence in the neck three months after right tongue-jaw-neck resection for carcinoma of the tongue.

Harris and Smith [*2*] found tumor cells in washings from approximately 25 per cent of a series of 107 operative cases of cancer of the head and neck. In a previous paper [*1*], we reported the recovery of cancer cells in 5.3 per cent of washings. The present report deals with an extension of this study, a partial follow-up of cases and the use of 0.5 per cent Clorpactin® XCB* as a wound irrigant in cases selected at random.

METHODS AND MATERIALS

Over a four and a half year period, January 1956 through June 1960, wound washings were obtained from 279 patients with cancer of the head and neck, and from fifty-one patients with benign lesions of the head and neck region. All the patients with malignant lesions had clinically operable lesions with or without regional metastases and the usual radical procedures were employed.

Before reconstruction and closure of the skin flaps, the wound was irrigated with 50 cc. of isotonic saline and the washings were collected in a basin and sent directly to the labora-

* Clorpactin XCB is the trade-mark of the Guardian Chemical Corporation for a brand of monoxychlorosene, a stabilized, buffered, organic derivation of hypochlorous acid.

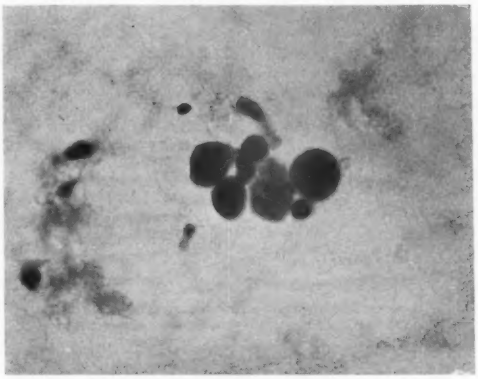

FIG. 2. Clump of tumor cells in smear from wound washings in a case of carcinoma of the floor of the mouth.

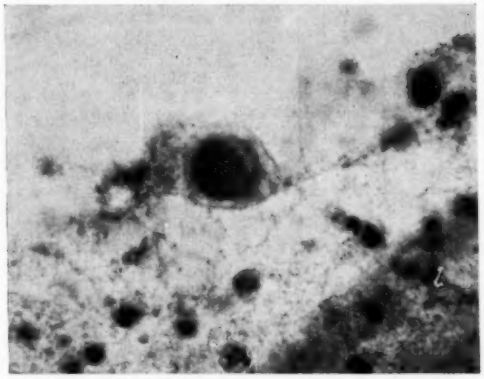

FIG. 3. Tumor cell in a smear from a wound washing from a carcinoma of the tongue.

tory in a glass container. Because processing was immediate, no fixative was added.

The washings were centrifuged for fifteen minutes at 2,000 r.p.m., the supernatant fluid was aspirated and two smears were made from the buffy coat of the sediment. The processing was by the standard Papanicolaou technic, the smears being fixed immediately in a solution of equal parts of alcohol and ether. After thirty minutes, the smears were stained with Harris's hematoxylin, OG-6, and EA 36.

In fifty-eight cases taken at random since April 1958, the wound was irrigated with a fine spray of 50 cc. of 0.5 per cent Clorpactin XCB, and the solution was allowed to remain in contact with the tissues for exactly five minutes before being flushed out of the wound with 300 cc. of isotonic saline. All cases prior to adoption of Clorpactin XCB, and all subsequent cases not receiving Clorpactin XCB, were irrigated with 300 cc. of saline. These cases served as our controls.

RESULTS

Table 1 shows the results of wound washings in 279 operable cases of cancer of the head and neck. There were positive cells in sixteen (5.7 per cent) and atypical cells in five (1.8 per cent) of the washings. The washings from fifty-one benign head and neck lesions were also studied, with negative results. The tumor cells were usually found in small clumps (Fig. 2) or as single isolated cells. (Fig. 3.)

In eleven of the cases with positive washings, the procedure was excision of the primary tumor together with regional nodes. Of the eleven cases, six had positive nodes. This group of positive washings is too small, however, for extensive analysis of the data to be meaningful.

The recurrence rate for 178 operative sites that had negative washings and have been observed for one year or longer has been 25 per cent. (Table II.) Forty-seven patients with negative wound washings received 0.5 per cent Clorpactin XCB and have been followed

TABLE 1
RESULTS OF WOUND WASHINGS FROM 279 OPERABLE CASES OF CANCER OF THE HEAD AND NECK

Site	No. of Cases	No. Positive for Cancer Cells	No. with Atypical Cells
Larynx	70	3	1
Pharynx and pyriform sinus	18	1	0
Maxillary antrum	11	7	0
Parotid gland	5	0	0
Submaxillary gland	2	0	0
Lip	2	0	0
Thyroid	10	0	1
Tongue	46	2	1
Tonsil	13	1	0
Floor of mouth	23	1	1
Retromolar area	5	0	1
Alveolar ridge	14	0	0
Buccal mucosa	4	0	0
Palate	4	0	0
Metastatic neck nodes	50	1	0
Nose	2	0	0
Total	279	16 (5.7%)	5 (1.8%)

TABLE II
LOCAL RECURRENCE IN WOUNDS WITH NEGATIVE WASHINGS AND ONE YEAR OR MORE OF FOLLOW-UP

Site	No. of Cases	No. of Recurrences
Larynx	48	5
Pharynx and pyriform sinus	9	3
Maxillary antrum	4	2
Parotid gland	3	1
Submaxillary gland	1	0
Lip	1	0
Thyroid	5	0
Tongue	31	9
Tonsil	9	4
Floor of mouth	15	2
Retromolar area	2	2
Alveolar ridge	8	2
Buccal mucosa	3	0
Palate	2	1
Metastatic neck nodes	35	13
Nose	2	0
Total	178	44 (24.7%)

TABLE III
RECURRENCES IN WOUNDS WITH NEGATIVE WASHINGS AND IRRIGATED WITH 0.5 PER CENT CLORPACTIN XCB

Site	No. of Cases	No. of Recurrences
Larynx	12	2
Pharynx and pyriform sinus	3	3
Maxillary antrum	0	0
Parotid gland	0	0
Submaxillary gland	1	0
Lip	1	1
Thyroid	4	0
Tongue	9	2
Tonsil	2	0
Floor of mouth	5	1
Retromolar area	0	0
Alveolar ridge	5	2
Buccal mucosa	0	0
Metastastic neck nodes	5	1
Nose	0	0
Total	47	12 (25.5%)

up for one year or longer, the local recurrence rate being 25.5 per cent. (Table III.)

In ten operative wounds that had positive washings and have been followed up one year or longer, there has been local recurrence in eight. In four operative sites with atypical cells found in the washings and with a follow-up of one year or longer, there has been no evidence of local recurrence. Two additional wounds that had positive washings and received 0.5 per cent Clorpactin irrigations have been observed for one year or longer, and there has been local recurrence in one.

COMMENTS

If local recurrence can be attributed to local implantation at the time of surgery, the discrepancy between the 5.7 per cent proportion of washings containing tumor cells and the 27 per cent over-all recurrence rate for 241 patients who have been followed up for one year or longer may be due to one or more of these possibilities:

1. Failure of our present washing and concentration technic to detect tumor cells in more than 21 per cent of the washings.

2. Implantation, in the raw wound, of tumor cells from lymphatic and blood channels that were cut across during the surgery and continue to ooze during the postoperative period.

3. Other factors which are not apparent but play a significant role in the incidence of local recurrence in head and neck cancer.

Our technic of collection and concentration is similar to that employed for our chest and peritoneal washings, for which the yields have been considerably higher and the methods have been found reasonably satisfactory. By this technic, Moore et al. [11] found that 50 per cent of all patients with colon, stomach and lung cancers had positive peritoneal and pleural washings.

Smith [9] has observed the presence of tumor cells in blood, lymph and tissue juices which continued to drain from the wounds forty-eight to seventy-two hours after surgery. In such instances, a single application of a topical chemotherapeutic agent which is allowed to be in contact with the wound only for a short time would be far from effective in preventing subsequent seeding in the wound.

Since we began clinical use of Clorpactin XCB, a number of papers have appeared in the literature, with considerable disagreement as to the relative efficacy of Clorpactin as an effective cytotoxic agent for animal tumors in experimental animals in concentrations which were regarded as safe for clinical use.

Gliedman et al. [12] found that Walker carcinosarcoma 256 and sarcoma 180 cells

suspended in 0.4 per cent and 0.5 per cent Clorpactin XCB did not grow after inoculation into the peritoneal cavity of rats and mice. Supravital staining showed that the sarcoma 180 cells were rapidly rendered nonviable in a solution of 0.5 per cent Clorpactin XCB. Thomas and his associates [13] reported that Clorpactin XCB at concentrations of 0.5 per cent and 1 per cent did not prevent tumor growth and ascites development, although a 2 per cent concentration was effective in 90 per cent of the animals.

Collier and his group [4] found that 0.5 per cent Clorpactin XCB was only slightly effective. Atek et al. [14] concluded that Clorpactin XCB was not useful in prevention of tumor-cell spread in tumors of the gastrointestinal tract in experimental animals. In animal experiments, Ketchum [6] found that a concentration of 1 per cent Clorpactin XCB or higher is necessary to effect a depression of tumor growth.

Clorpactin XCB is being employed clinically by a number of investigators [4,8,15] but no definite evidence of its effectiveness in preventing seeding and local wound recurrence is yet available.

Collier et al. [4], having noted systemic manifestations in dogs with the use of 2 per cent solutions, have been irrigating surgical wounds in clinical practice with 250 ml. of 1 per cent Clorpactin XCB every forty-five minutes during the operation, and with 500 ml. at the end, as well as washing and soaking the hands for three minutes.

Our results with irrigations of wounds with 0.5 per cent Clorpactin XCB have been disappointing. The recommended concentration may be ineffectual *in vivo*, as shown in tumor systems in animals. At the present time, however, the results of our wound washings tend to make us feel that the percentage of patients who might benefit would be quite small. In cases with negative washings, subsequent local recurrence may be due to factors other than operative seeding, and hence the patients would conceivably not be benefited by a topical cytotoxic agent such as Clorpactin XCB, whose main purpose is to destroy desquamated cells.

SUMMARY

1. Cancer cells were found in washings from sixteen of 279 radical operative wounds for head and neck cancer. In five washings, atypical cells were seen. No false positive or suspicious cells were found in washings from fifty-one benign head and neck lesions.

2. Our recurrence rate in 178 operative sites with negative washings and a follow-up of one year or more has been 25 per cent.

3. In fifty-eight cases selected at random with negative washings, 0.5 per cent Clorpactin XCB has been used as a wound irrigant. In forty-seven cases which have been followed up one year or more, the local recurrence rate has been 25.5 per cent.

4. Local recurrence has been found in eight of the ten patients who have had positive washings and have been followed up for one year or longer.

5. In one of two patients who had positive wound washings and received 0.5 per cent Clorpactin XCB irrigation has developed local recurrence during a follow-up of one year or longer.

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Squamous Carcinoma of the Oral Cavity and Throat

ITS CLINICOPATHOLOGIC CORRELATION

RUSSELL P. SHERWIN, M.D. AND ANTHONY ZOVICKIAN, M.D., F.A.C.S., *Boston, Massachusetts*

From the Departments of Pathology and Surgery, The Boston University and Massachusetts Memorial Hospital Medical Center, Boston, Massachusetts.

IN CURRENT practice, the morphology of epithelial tumors of the oral cavity and throat receives little clinical application. This is due to an underemphasis of pathologic factors which have prognostic and therapeutic importance. These factors include warty or papillary structure, associated *in situ* carcinoma, depth of invasion, vascular invasion and evidence of "host resistance." The underemphasis of these details has resulted in the tendency for both pathologist and clinician to accept the diagnosis of epidermoid carcinoma unqualified, except for a grade number. This study emphasizes morphology and its importance particularly in relationship to prognosis.

Of eighty-five head and neck cancer cases, seventy-five were suitable for histologic study, having sufficient microscopic slides or paraffin-embedded tissue. Seventy-two cases were adequate for clinical correlation. The clinical information was supplied by one surgeon, Dr. Anthony Zovickian, who had given either complete or partial care in all of these cases. The patients were treated at four different hospitals between 1953 and 1959. The anatomic locations of primary sites of cancer studied were tabulated. (Table 1.) All but one received major surgery either alone or in combination with radiation therapy. The principle of the composite resection and immediate repair was carried out in all applicable cases. A follow-up examination ranged from thirty-two to eighty-four months.

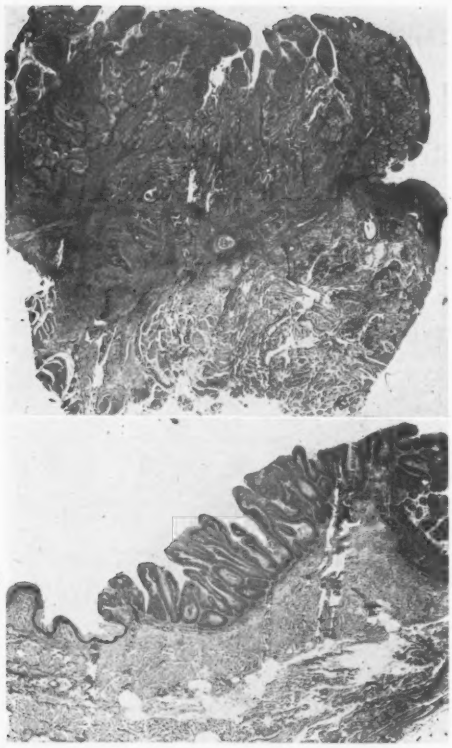
A list of standard, established pathologic factors to evaluate prognosis was compiled:

TABLE 1
ANATOMIC LOCATIONS OF LESIONS

Primary Site	No. of Cases
Lip	7
Lip commissure and buccal mucosa	1
Buccal mucosa	1
Gingival, buccal, mucosal sulcus	2
Gingiva	3
Mandible—ramus	1
Retromolar region	2
Palate and upper jaw	3
Antrum	1
Floor of mouth	11
Tongue—anterior third	1
Midlateral	3
Base	9
Tonsil	6
Epiglottis	7
Epilarynx	5
Pyriform sinus	8
Intrinsic larynx	6
Hypopharynx	3
Neck	3
Total	83*

* The increase over the total number of cases studied is due to those cases which had more than one primary site of carcinoma.

1. Pattern of the tumor
   - A. Depth of invasion
   - B. Vascular and lymphatic invasion
   - C. Cytology (anaplasia)
   - D. Post-therapy findings:
     1. X-ray response
     2. Surgical margins (including multicentricity, residual tumor and precancerous change)



1A

1B

FIG. 1. Exophytic verruciform carcinoma. A, there is a wart-like pattern and, on higher magnification, the cells show slight to moderate anaplasia. Note the relatively straight line of invasion and the dark band of lymphocytes beneath the tumor margin and the mucosa on the right. This patient had an *en bloc* radical resection for carcinoma of the base of the tongue and epiglottis with cervical lymph node metastases. Recurrence in the pharynx twenty-seven months later was treated by external radiation. He is living sixty-seven months after resection, without evident recurrence and is well. B, papillary exophytic carcinoma, the tumor is relatively superficial here but more invasive elsewhere. There are some villous-like fronds; the epithelial pegs are broad and the cells are very well differentiated. This lesion resembles Ackerman's verrucous carcinoma [1,2] but has less evident fronds. The patient had a buccal tumor which recurred four years later. She has been free of disease for ten months following the second resection.

II. Host resistance factors (unknown)
   - A. Lymphoid stroma
   - B. Basement membrane dissolution
   - C. Tumor necrosis
   - D. Foreign body type granulomatous response (as in homotransplant)
   - E. Polyploidy

TABLE II
CLINICOPATHOLOGIC CORRELATION

Type and Statistics	No. of Cases
Verruciform carcinomas	
Exophytic	5
Endophytic	4
Squamous and epidermoid carcinomas	
Correctly predicted and patient living without disease	3
Incorrectly predicted and patient living without disease	12
Correctly predicted and patient dead	21
Incorrectly predicted and patient dead	2
Adenocarcinomas	4
Undifferentiated carcinomas	5
Transitional carcinomas	3
Pseudosyncytial (tonsillar) carcinomas	2
In situ carcinomas ± superficial invasion	3
Pseudocarcinoma (erroneous diagnoses: acanthosis and metaplasia)	2
Miscellaneous (incidental deaths without autopsies, metastatic disease originally interpreted as primary or problem of two primary diseases, patients living with recurrence)	6
Total	72

The study of lymphatic and vascular invasion was discontinued because appropriate sections and special stains were not available in all cases. The presence or absence of *in situ* carcinoma was specifically recorded for two reasons: First, to establish that a tumor is primary and secondly, to distinguish between primary and secondary recurrence.

In order to reproduce the original clinical situation as closely as possible for the purpose of predicting prognoses, the slides were selected by the surgeon and submitted to the pathologist in chronologic order. The first fifteen cases were tabulated without reference to the clinical history. Then the patient's records and the predicted clinical courses were compared. After this initial study, each case was discussed immediately after the slide review. At the end of the study, all of the slide material was studied again.

RESULTS (TABLE II)

Two patterns of tumor structure were found to be of most use in predicting the clinical course: (1) a bulky squamous cell tumor, either

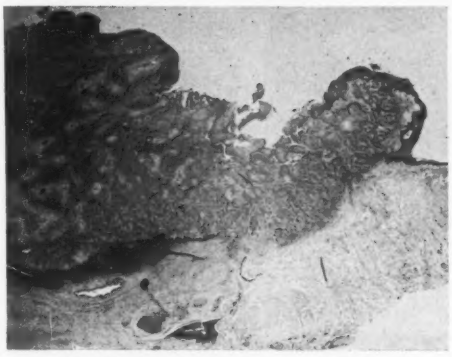


FIG. 2. An endophytic type of verruciform carcinoma. Note the crateriform effect and the overhanging mucous membrane margin on the right side. Note also the dark bands of lymphocytic infiltrate at the advancing margin and within the tumor mass. The lesion arose from the floor of the mouth. The patient is free from disease eighty-four months following radical *en bloc* resection and immediate replacement of lining membrane. Note: This is *not* the verrucous carcinoma described by Ackerman and was initially called unfavorable because of its pleomorphism and the deep invasion.

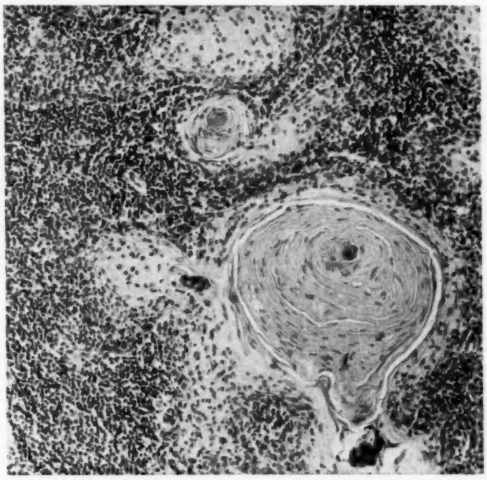


FIG. 3. A squamous carcinoma invading skeletal muscle. The cytology is fairly uniform. The presence of prickles obviates the term epidermoid. The patient had widespread visceral metastases.

endophytic or exophytic and verruciform in nature (Figs. 1 and 2), included is the so-called verrucous carcinoma [1,2] which we interpret as a special form, papillary type, of the exophytic carcinomas; and (2) infiltrative epidermoid or squamous cell islands of small size. The first group was favorable; the second (Fig. 3), with a few exceptions, was a group with an unfavorable outcome. The presence or absence of stromal proliferation was not a helpful factor.

Nine cases of verruciform cancer were found of which four were exophytic, including two verrucous carcinomas, and five were endophytic. Five patients, as predicted, are living and well without tumor recurrence. The locations of tumors and length of time patients lived are as follows: larynx, thirty-three months; lip, thirty-six months; jaw, forty-eight months; tongue and epiglottis, sixty-seven months and floor of mouth, eighty-four months. Two cases were considered unfavorable because of (1) extensive local infiltration and (2) the presence of two tumor types, one of which was undifferentiated. Both patients died after local recurrence several months after surgery. An eighth case of verruciform cancer showing focal, deep and isolated invasion was called unfavorable; however, the patient is free of recurrence thirty-eight months following total laryngectomy. In the ninth case despite a favorable prediction the patient died of carotid artery hemorrhage after local recurrence. There was an interval of nine months after radiation before surgical extirpation was accepted and performed.

Of thirty-eight cases of invasive squamous or epidermoid carcinoma, twenty-one were correctly interpreted to show an unfavorable course. Three of the thirty-eight were considered favorable; two showed an extraordinary lymphocytic infiltrate about extensively necrotic tumor masses (Fig. 4) and one was superficially invasive. Another case of lymphocytic response was called favorable despite lymph node metastases but the patient died of local disease. Another error was a very well differentiated tumor with a broad margin and abundant keratin that metastasized to the lungs. (Fig. 5.) One tumor was thought to have arisen from a branchial cleft. Two cases with less impressive lymphocytic infiltrate (one of these with a foreign body type of granulomatous reaction to the tumor) were considered unfavorable. One of these cases had two tumor types and in the other case the tumor was located deep in the submucosa, suggesting inclusion cyst origin. The patient in the first of these two cases had three recurrences from a base of the tongue cancer, but is now free of disease

FIG. 4. A squamous carcinoma with marked lymphocytic infiltrate. The other outstanding finding is the fading or slow necrosis of tumor cells. Note that a basement membrane cannot be identified. Most of the tumor mass is made up of keratinizing cells. This is an excellent example of the "host resistance" phenomenon. The lesion arose from the midlateral tongue. A composite operation was performed, replacing the oral cavity lining with a skin graft. The patient is free from disease seventy-four months following surgical treatment.

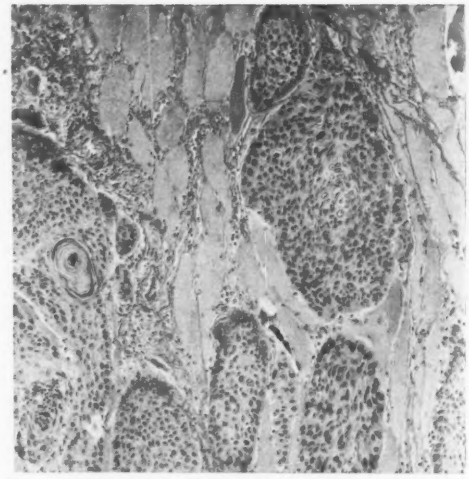


FIG. 5. Infiltrating, well differentiated squamous cell carcinoma of the epiglottis which metastasized to the lungs. A cellular response is absent.

seventy-two months after the last recurrence. The patient in the second case is alive thirty-seven months following resection of a floor of the mouth cancer. These cases also called unfavorable, but free of disease, showed a marked lymphocytic response and, in addition, four of the nine showed a foreign body type granulomatous response (Fig. 6). Nine patients had the following location of tumors and survival time: Retromolar (seventy-two months), gingiva (seventy-two months), floor of mouth (two cases: thirty-seven months and autopsy without residual tumor), extrinsic larynx (two cases: sixty-two months and autopsy at thirty-two months without residual tumor), hypopharynx (seventy-two months), tongue (forty-two months), and lip (fifty-two months). Four of the nine cases had positive lymph nodes. Granulomas were not found in any other tumors of the series. A marked lymphocytic stroma was found in all but one of the verrucous carcinomas. Lymphocytic reaction was not prominent nor was it present in the cases with unfavorable outcome, with the exception of the few instances mentioned.

Two cancers originally diagnosed as squamous and epidermoid types were shown to be adenocarcinomas. One was undifferentiated except for rare acinar formation and the other was of glandular origin (mucoepidermoid tumor). The patient who had mucoepidermoid tumor is living and well thirty-two months postoperatively without recurrence, and the patient with the rare acinar formation died of metastatic disease.

Other significant observations were these: (1) Three carcinoma *in situ* cases, one of which was not invasive, a second which was just superficially invasive and a third which showed extensive *in situ* carcinoma but, in addition, had focal invasion with lymph node metastasis. The patient in the latter case, is still free of disease thirty-four months after operation. (2) One case of verrucous carcinoma had a prior biopsy interpreted as keratoacanthoma [3] which emphasizes the need for knowledge of the entire lesion, clinical and pathologic. (3) A case of marked sialadenitis with leukoplakia of surface epithelium and benign epidermidization of deep ducts and glands, resembling well differentiated squamous cancer and diagnosed as such. The clinical diagnosis was abscess of the palate but the pathologist, on direct questioning, says he was not aware of this at the time.

COMMENTS

We wish to emphasize that no statistical analysis of this relatively small series has been attempted, and it is self-evident that no one factor is all important. Nevertheless, over one half of the cases with a favorable outcome were readily identified on the first review, and only a few errors were made in the selection of those cases with poor prognoses. Although Ackerman's verrucous carcinoma is not a common oral cancer, we hope this study will add support to his strong attempt to gain recognition for this rather neglected entity.

"Host resistance" factors have not been clearly defined. The generally accepted feature is the presence of a dense lymphocytic stroma as with seminoma of the testis and medullary breast cancer. However, there appears to be additional supporting evidence, namely, a foreign body type giant cell response. The latter, interestingly enough, seems to be identical with the fate of homotransplants and has not been described previously in human tumors. We have seen this response in some lung cancers as well. In addition, the study suggested that bizarre nuclear forms (particularly polypoidy) are also a sign that the tumor is growing with difficulty, and need not be interpreted as ominous. We did not find Broder's grading useful except in the sense that all of the undifferentiated carcinomas were unfavorable. Contrariwise, three of our most differentiated squamous cancers (epiglottis, larynx and floor of the mouth) metastasized widely. The case of adenocarcinoma that survived had a differentiated adnexal pattern; the prediction was "probably favorable." It should be noted that the Broder grading is not uniformly applied and that some laboratories use only three grades.

In situ carcinoma has four significant aspects. Two of these, multicentricity and extensive surface involvement, are well known [4]. Two others have received less attention. They are the relationships of *in situ* carcinoma to primary tumor identification and to three forms of recurrence. *In situ* cancer, in continuity with invasive cancer, is proof that a tumor is primary. In view of the high incidence of *in situ* cancer in this series of cases, without the benefit of all of the original material, little difficulty should be expected in ruling out metastatic disease. Recurrent invasive cancer with *in situ* cancer in continuity indicates either a new disease or progression of incompletely removed *in situ* cancer. Recurring invasive cancer without *in situ* cancer means inadequate primary excision or metastasis. The use of frozen section to evaluate tumor margins where *in situ* cancer may exist should be encouraged.

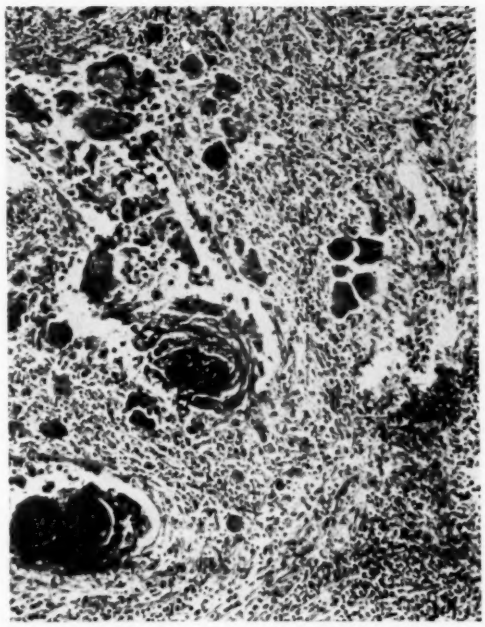


FIG. 6. Marked tumor necrosis of a squamous carcinoma of the right aryepiglottic fold and pyriform sinus, metastatic to cervical lymph nodes. Both the primary tumor and the metastasis showed extensive tumor necrosis with numerous foreign body giant cells about keratinous masses and remnants of tumor cells. This patient had local recurrence three years after radical surgery but is living with disease four years later.

For standardization purposes we suggest that the following terms be used:

1. Squamous carcinoma: Polygonal cells with prickles or with unequivocal and frequent pearl formation.

2. Epidermoid carcinoma: Polygonal cells with vague or absent prickles, and without pearls and keratin. A basal cell dominance is usually present, and the cells may approach spindle cells.

3. Transitional cell carcinoma: Round cells without prickles or pearls, resembling the epithelium of the urinary bladder. Clear cells

FIG. 7. This is a mixture of tumor types, a bulky transitional cell carcinoma within a dilated ductlike structure (*left side*) and numerous ductlike channels whose lining is epidermoid and squamous (*right side*). Note the nipple-like effect created by the numerous ducts rising to the surface (*top right*). *In situ* carcinoma involves a small portion of the surface epithelium. Patient is living and free from disease sixty-two months following laryngectomy, partial pharyngectomy and right radical neck dissection. Primary site of cancer was extrinsic larynx.

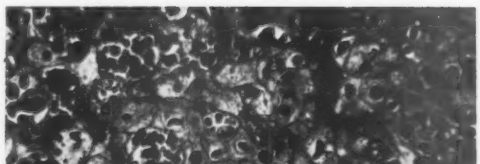


FIG. 8. Transitional cell carcinoma characterized by round cells having abundant cytoplasm. The cells on the left half of the photograph show abundant intracytoplasmic droplet formation. This tumor arose from the neck, exact primary site undetermined. The patient died of lung metastasis within eight months. This cancer is similar in type to those neoplasms described as ductal in origin [5]. They are considered highly aggressive.

may occur. The term "ductal carcinoma" should be replaced by "papillary and cystic forms." (Figs. 7 and 8.)

4. Pseudosyncytial cell carcinoma: Sheets of cells without well defined cell boundaries, similar to the epithelium of the normal tonsillar crypt. No differences in behavior between this type of tumor and those of the surface epithelium were noted. Two of the five tonsillar cancers showed this type of epithelium, and we were able to identify a recent tonsillar cancer (not in this series) by this pattern. The pattern was not found outside of the tonsillar area.

Combinations of tumors occur fairly often, although one type usually predominates. The most mature (differentiated) area should be the basis for diagnosis, using other areas to qualify the designation. In some cases differences between the biopsy material, resection specimen and recurrences suggest a change of pattern, but the original material often has matching areas. One case in this study, however, exhibited a different and more benign pattern on recurrence which was additional support for a new disease rather than recurrence. Changes following x-ray examination were either unnoticeable or minor, the cells enlarging and polyploidy increasing. Necrosis, however, was occasionally extensive and associated with neutrophil infiltration. Of interest is the fact that lymphocytic stroma appears to be partially lost in the acute response to radiation therapy but may be marked in the postradiation period.

Lastly, there is the problem of communication between clinician and pathologist. It is worth emphasizing that the use of the pathology department as a consulting, rather than a laboratory service, will lead to a better understanding of both the clinical and the pathologic problems. In particular, the pitfalls of a nonrepresentative biopsy, the poor orientation at frozen section and the incomplete pathologic diagnosis are all amenable to a mutual interest.

SUMMARY

1. This study of seventy-five cases of oral cavity and throat cancers correlates the histopathology with prognosis as it relates to major surgical resection.

2. Major surgical resection, with and without x-ray therapy, appears to be more effective when the cancer is bulky or verruciform. On the other hand, squamous and epidermoid cancers, with and without differentiation, and with an infiltrative pattern, generally have had very aggressive courses. The presence of a marked lymphocytic stroma and foreign body type of granulomas with tumor necrosis is evidence for a more favorable outcome with major resection.

3. The need for a standardization of terms and improved liaison between the clinician and pathologist is stressed.

Acknowledgment: We wish to express our appreciation to the following who graciously made available the material necessary for this study: Werner Mueller, M.D., Director of the Mosher Laboratory, The Massachusetts Eye and Ear Infirmary, Boston; John J. Byrne, M.D., Director of the Third (B.U.) Surgical Service, Boston City Hospital; G. Kenneth Mallory, M.D., Professor of Pathology at Boston University School of Medicine; and Harold W. Harrower, M.D., Chief of Surgical Services, Veterans Administration Hospital, Providence, R. I.

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Palliation Achieved in Carcinoma of the Head and Neck with Intra-Arterial Chemotherapy

CALVIN T. KLOPP, M.D., DAVID FORSYTHE SMITH, M.D. AND T. CRANDALL ALFORD, M.D.,
Washington, D. C.

From the Department of Surgery, George Washington Univ. School of Medicine, Washington, D. C.

IN 1950 a method of intra-arterial chemotherapy for palliation in patients with nonresectable carcinoma of the head and neck was described [4]. With the use of this localized therapy to regionally confined tumors employing HN2 significant local regression was produced without the development of systemic toxicity. By fractionated administration of the total dosage a better therapeutic effect was achieved. The results obtained were beneficial but of too short duration to justify extended use. This basic procedure of regional intra-arterial therapy has now been modified and extended. In 1957 Creech et al. [1] used an extracorporeal pump to circulate agents through the vascular channels within regions infiltrated with carcinoma. They hoped to confine the chemotherapeutic agent within the region perfused and to eliminate systemic toxicity. However, the technic has been successful mainly with malignancy involving an extremity [2,6]. In perfusions in other regions complete circulatory isolation was not possible and leakage of the agent into the systemic circuit limited the effectiveness [1,7].

In 1959 Sullivan [8] reported the use of continuous slow intra-arterial infusion of an antimetabolite (methotrexate). Systemic toxicity was minimized or prevented by parenteral administration of a protective agent (citrovorum factor). In all ten patients with recurrent epidermoid carcinoma of the head and neck initially treated in this fashion, definite relief from pain and objective tumor regression was noted. In a later series [9] of twenty-seven patients partial tumor regression was noted in twenty-one and total tumor regression in five. However, neither the extent nor duration of regression was clearly described.

Inasmuch as both regional perfusion and continuous arterial infusion are more complicated and expensive than fractionated intra-arterial therapy it seemed of value to determine the comparative effectiveness of these three technics. To do this we have reviewed the results obtained in all patients with carcinoma of the head and neck treated with fractionated intra-arterial HN2 over the past ten years and a smaller series recently treated with the continuous methotrexate intra-arterial infusion technic. As our experience with the isolation perfusion technic has been limited we have evaluated this procedure by a review of the literature.

ISOLATION PERFUSION

In most instances perfusion technics [3] now utilize alkylating agents and antibiotics. An external carotid perfusion is performed while venous return utilizes the common facial or the internal jugular vein. All anterior and lateral veins are ligated. The leakage factor is rarely lower than 75 per cent.

The results from this technic have not been impressive. Woodhall [10] reported twenty-one of twenty-two patients receiving subjective relief from pain with varying degrees of tumor regression for periods up to six months. More recently he [11] reported twenty cases in which he achieved marked regression in three patients, moderate regression in eight patients, five of whom did well until recurrences developed in three to six months. All patients had complete pain relief. Duration of remission had not exceeded six months in any reported series.

METHOTREXATE INFUSION

We have treated nine patients with nonresectable carcinoma of the head and neck by

TABLE I

RESULTS IN NINE PATIENTS WITH CARCINOMA OF THE HEAD AND NECK

Patient	Age (yr.) and Sex	Diagnosis	Previous Treatment	Vessel Used	Treatment (days)	Dosage Methotrexate (mg.)		Dosage Citrovorum Factor		Toxicity	Immediate Results		Length Response (days)	
						Daily	Total	Daily	Total		Objective	Subjective	Objective	Subjective
W. D.	56,M	Epidermoid carcinoma of nasopharynx, with metastasis to neck	Surgery and x-ray	External maxillary	5	10–25	95	36	180	None	20% regression	Complete pain relief	40	60
D. B.	78,M	Muco-epidermoid carcinoma of base of tongue	Surgery	Superior thyroid	4	30	120	24	96	None	None	None	0	0
R. P.	65,M	Epidermoid carcinoma of parotid gland	Surgery and x-ray	Superior thyroid	4	40	160	24	96	None	None	None	0	0
P. S.	60,M	Epidermoid carcinoma of soft palate with extension into the nasopharynx	X-ray and surgery	Superior thyroid	7	60	420	24	168	Leukopenia; stomatitis	90% regression	Complete pain relief	60	60
					(Second course) 3	50	150	18	48	None	Nasopharynx None	None	0	0
E. W.	65,M	Epidermoid carcinoma of base of tongue and pharynx	Surgery	Superior thyroid	9	75	675	36	324	Edema of tongue; stomatitis	40% regression tongue	Complete pain relief	40	50
E. R.	65,M	Epidermoid carcinoma of the mastoid	X-ray	Lingual	6	100	600	24	144	Leukopenia; stomatitis	25% regression	Complete pain relief	30	30
					(Second course) 3	75	225	12	36	None	None	No pain relief	0	0
B. M.	38,F	Epidermoid carcinoma of the maxilla	Surgery	Lingual	5	100	500	24	120	Leukopenia; pharyngitis	90% regression	Complete pain relief	150	150
					(Second course) 5	50	250	12	60	Pharyngitis	100% regression	Complete pain relief	30	30
J. F.	55,M	Epidermoid carcinoma of the floor of the mouth	None	Bilateral	5	100	500	36	180	Leukopenia; stomatitis	20% regression	Asymptomatic	28	Not applicable
				Superior thyroid	3	100	300	36	108	Escherichia coli; septicemia				
					(Second course) 1	100	100	12	12	None	0	...	0	0
E. S.	55,M	Epidermoid carcinoma of tongue	Surgery and x-ray	External carotid	5	50–100	400	24	120	Stomatitis; severe edema	10% regression	?Pain No relief	10	0

TABLE II

TREATMENT OF HEAD AND NECK MALIGNANCY WITH INTRA-ARTERIAL NITROGEN MUSTARD

Patient	Age (yr.) at Onset	Disease and Location	Original Treatment	Date of Recurrence	Days	Dosage of Intra-arterial HN_2	Mg./Kg.	Total mg.	Patient's General Condition	Gross Objective Remission	Subjective Remission	Length of Remission (days)	Leukopenia (below 4,000)	Radiomimetic Changes	Clinical Course	Vessel Cannulized
J. H.	70	Epidermoid carcinoma of upper lip; metastases to submaxillary gland	Surgery and x-ray	3 mo.	11	1.3 mg./8 hr.	1.47	76.7	Poor; severe pain	Decrease in tumor size; partial healing	Control of pain	89	1,200	Erythema of face; swelling of tongue and salivary glands	Died in 89 days	Superior thyroid
J. S.	75	Epidermoid carcinoma of soft palate	Surgery	Cervical 8 mo.	22	1.1 mg./24 hr. then every 12 hr.	1.1	41	Poor; severe pain	Decrease in size	Control of pain	25	None	Muscositis of pharynx and soft palate	Died in 25 days	Lingual and superior thyroid
L. L.	57	Epidermoid carcinoma of antrum; metastases to submaxillary gland	Surgery and x-ray	9 mo.	12	1.5 mg./12 hr. (second course in 4 days)	0.53	39	Poor; severe pain	Decrease in size	Control of pain	33	None	Mucositis of soft palate; facial erythema	Died in 33 days	Lingual and superior thyroid
					7	2 mg./8 hr.	0.55	41								
V. S.	63	Epidermoid carcinoma of antrum	None	Palate, orbit and ethmoids	11	1.5–2/8–12 hr.	0.9	57	Fair; persistent headache	Decrease in size	Control of pain	26	800	Mucositis; dysphagia; erythema and edema of face	Died in 26 days	Superior thyroid
C. G.	79	Epidermoid carcinoma of mouth	None	6 mo.	7	5 mg./12 hr. (second course in 15 days)	0.23	15	Fair; no initial pain; subsequent pain relieved by second course	...	Control of pain	38	450 second course	Hyperemia of face and pigmentation	Died in 38 days	Superior thyroid
					9	2 mg./8 hr.	0.76	50								
D. M.	84	Epidermoid carcinoma of antrum	None	...	7	1 mg./8 hr.	0.36	20	Good; mild pain	Decrease in size	Control of pain	4 mo.	None	Erythema; mucositis of palate	Died in 4 mo.	Lingual
B. B.	72	Epidermoid carcinoma of floor of mouth	Surgery	3 mo.	6	1 mg./8 hr. (second course in 13 days)	0.2	16	Fair; severe pain	Decrease in size	Control of pain	7 wk.	None	Mild mucositis; erythema of face	Died in 7 wk.	Superior thyroid
					7	5 mg./8 hr.	0.12	10								
F. W.	51	Epidermoid carcinoma of larynx	None	Bilateral, large cervical nodes	8	2 mg./8 hr.	0.8	48	Poor; severe pain	None	Relief of pain	14	...	Mucositis	Died in 2 wk. of bacterial endocarditis	Bilateral external carotid; bilateral thyrocervitis
D. W.	42	Epidermoid carcinoma of tongue	Surgery and radium	Bilateral cervical nodes in 4 mo.	7	1 mg./8 hr.	0.4	20	Fair; severe pain	Regression of tumor and nodes	Control of pain	4 mo.	None	Tumor hem. mucositis-edema-tongue	Died in 5 months	External carotid bilateral
C. S.	57	Epidermoid carcinoma of tongue	None	Cervical nodes	9	1 mg./8 hr.	0.35	26	Fair; pain	Regression of tumor and nodes	Control of pain	2 mo.	None	Tongue edema	Died in 2 months	External carotid bilateral
B. G.	75	Epidermoid carcinoma of larynx	Surgery	Neck	3	1.25 mg./12 hr.	0.15	10	Good; pain	Regression of tumor	Control of pain	9 mo.	None	Mucositis and epilation	Remission 9 mo.	External carotid

this method. (Table I.) The procedure used is that described by Sullivan [8]. A No. 18 polyethylene catheter was inserted into the external carotid artery and a continuous methotrexate infusion was given using a Byrd infusion pump. Concurrently citrovorum factor was given intramuscularly every four to six hours until completion of therapy. Therapy was continued four to ten days and from 100 to 675 mg. of methotrexate was given. Catheters were left in place when possible if subsequent therapy was indicated.

Only two of nine patients received significant regression and in each instance there was prompt recurrence within sixty days. Four patients were given a second course of therapy. Of these only one received a second response. This lasted five months and was a recurrent carcinoma of the maxilla. All patients achieved relief of pain which persisted until tumor recurrences became evident. Local complications ranged from mild edema to severe ulceration and necrosis and marked swelling in normal tissue. Systemic toxicity manifested by leukopenia and stomatitis occurred in the six patients who received more than 400 mg. of methotrexate. The dosages of methotrexate employed in this series were markedly greater and without an increase in citrovorum factor than in the series reported by Sullivan [8,9]. However the results do not approximate those reported by him.

FRACTIONATED INTRA-ARTERIAL HN2 INFUSION

Thirteen patients with determinate, recurrent nonresectable carcinoma of the head and neck have been treated by this method. (Table II.) Injections were given through a polyethylene catheter inserted into the appropriate artery supplying the tumor. From 1 to 1.5 mg. of HN2 was given every eight to twelve hours until evidence of bone marrow depression was apparent. Total dosage varied from 20 to 77 mg.

All patients achieved immediate relief of pain for durations varying from one to nine months. In nine of thirteen patients the tumor regressed to 50 per cent of its original size, while in three patients total remission occurred for periods of four to nine months. Side effects from this therapy ranged from mild local mucositis and edema to necrosis of small amounts of normal tissue.

COMMENTS

It would appear then that from the literature and data presented, isolated perfusion technics for carcinoma of the head and neck as performed today offer no real advantage over the method of fractionated intra-arterial HN2. The marked leakage factor attendant with head and neck perfusion does not permit adequate protection against systemic toxicity and limits the effectiveness of treatment in the perfused region. The reported results appear no better than those obtained by fractionated intra-arterial infusion. Both technics have been equally effective in controlling severe pain for which the simpler technic is certainly indicated. In addition, the perfusion technic is more traumatic, expensive, time-consuming and complicated. Consequently it is doubtful that the extensive surgery involved in perfusion is justifiable as a method of palliation, although it is useful as an experimental tool.

Methotrexate infusion in our experience has been less effective than fractionated intra-arterial HN2. The duration and degree of response have not been impressive nor has the duration of pain relief. Lack of tumor sensitivity to this antimetabolite may have been the basis of our failure or possibly the normal or necrotic tissue in the infused region provided adenine or other metabolites which permitted normal cellular metabolism even in the presence of the antimetabolite [5]. With the exception of one patient, it has been our impression that resistance to the antimetabolite soon developed and further regression was prohibited.

As regards local and systemic toxicity, the comparison of the fractionated with the methotrexate infusion reveals that local toxicity is comparable in each.

Continuous infusion while less complicated and expensive than perfusion is still more time-consuming and expensive than the fractionated intra-arterial HN2 therapy.

Our results with methotrexate infusion are not comparable with those reported by Sullivan [8,9] and perhaps the discrepancy between the two series may be explained by a difference in the criteria for evaluation. This also may be related to the selected of cases. For example, it has been our impression that small lesions containing a minimal amount of necrotic tissue exhibited the best response to antimetabolite

therapy. This was true in our two patients receiving near total regression.

SUMMARY

1. Palliation of nonresectable carcinoma of the head and neck is presently most easily achieved with fractionated dosages of intra-arterial HN2.

2. The technic of isolation perfusion in carcinoma of this region is neither indicated nor justifiable with the technics and chemotherapeutic agents presently in use except as an experimental tool.

3. Methotrexate infusion has been inferior to fractionated HN2 in our experience as regards both duration and extent of tumor regression and the duration of pain relief.

Fibrous Dysplasia of the Facial Bones

CLIFFORD L. KIEHN, M.D., JOHN D. DESPREZ, M.D. AND ALVIN H. HARRIS, M.D., *Cleveland, Ohio*

From the Surgical Service, University Hospitals, and St. Luke's Hospital, and the Department of Surgery, Western Reserve University School of Medicine, Cleveland, Ohio.

SINCE the original descriptions by Lichtenstein in 1938 [1], and again in 1942 [2] with Jaffe, of the several forms of fibrous dysplasia, numerous reports have appeared in the literature further documenting this disorder. Unfortunately, the authors mentioned have not been entirely successful in their attempt to remedy the confusion arising when various terms signifying distinct pathologic entities, such as osteitis fibrosa, osteofibroma, ossifying fibroma, were used interchangeably with fibrous dysplasia [3,4]. Thus, one result of the many reports is the obscuring of the natural history of and, consequently, the appropriate therapy for this particular fibro-osseous disorder. We would like to define this entity briefly and discuss certain features of its management, using as examples specific representative cases.

Fibrous dysplasia is a disorder of uncertain origin although various theories about its causes have been advanced including trauma [5] and congenital rests. In this disease there is an overgrowth of fibrous tissue extending outward from the medullary cavity, disturbing the normal architecture and frequently distorting the involved bone. It is classified according to the number of sites involved, namely, mono- or polyostotic, approximately 5 per cent of the latter type being further marked by the presence of hyperpigmentation and precocious puberty in girls [16]. Grossly, the lesion appears as gray yellow, rubbery tissue which distends the cortex of the involved bone. The histologic pattern (Fig. 1) shows one of the spicules of osseous tissue embedded in a fibrous matrix. The lesion is often first suspected in a young patient presenting with a firm, painless swelling of the involved bone [7]. The roentgenogram [8,9] taken to investigate the complaint revealed a multiloculated radiolucent area within the bone with hazy "ground glass" appearance. Not infrequently the lesion may be noted in an incidental x-ray [10]. Serum chemistries, including calcium, phosphorus and alkaline phosphatase, are within normal limits. The usual lesion is stated to progress slowly, if at all, causing little difficulty, and to become quiescent at about the time of puberty [11]. The management of such cases is simple observation. That not all cases behave so innocuously is also well known and surgical procedures from local excision to wider resections have been described [12–14].

The patients in Table 1 have all been operated on by one of us (C. L. K.) and the diagnosis established histologically. All patients noted the onset of the disease in childhood, the two older patients noting the appearance of the lesions fifteen and eight years, respectively, prior to their surgery. The presenting signs included swelling and facial distortion accompanied by pain in two instances. The facial

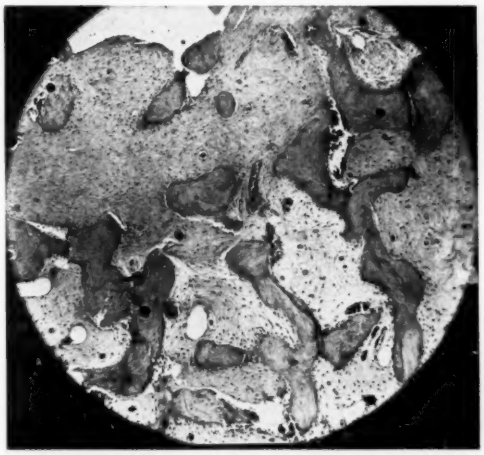
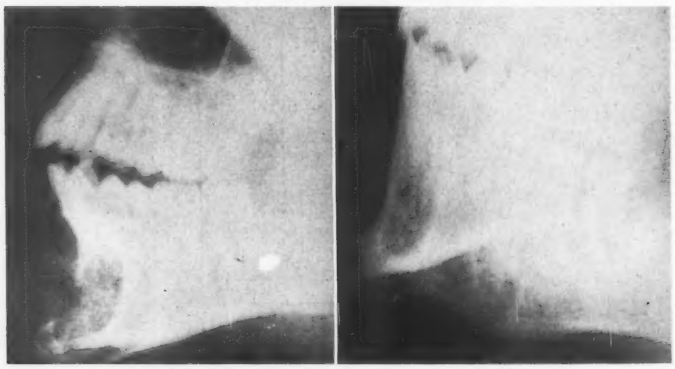


FIG. 1. Photomicrograph of typical lesion with osseous spicules in fibrous stroma. Original magnification × 50.



2A 2B

FIG. 2. A, preoperative lesion of symphysis of mandible. B, ossification occurring eighteen months following curettage.

bones noted were the only ones involved. The boy, aged five, and the girl, aged seven were brother and sister and presented examples of a familial form of fibrous dysplasia termed cherubism, a phrase first used by Jones in 1932 [*15,16*].

Pain and deformity were the indications for surgery. The operative procedure carried out in these five patients was currettage of the involved area with primary closure using an intraoral approach. This procedure also served as a biopsy in several of the patients. Follow-up examination of all the patients except one revealed healing and filling in of the bony defects. The asymptomatic recurrence noted in the first patient occurred in the fifth year after the original surgery and the patient has been followed up without operation, lack of progression being the indication for conservative management.

TABLE I
FIVE PATIENTS TREATED BY INTRAORAL CURETTAGE ONLY

No. of Patients	Involvement	Symptoms and Signs	No. of Operations	Follow-up
29 ♀	Mandible	Pain, facial asymmetry	1	6 yr., asymptomatic recurrence
14 ♂	Mandible	Swelling	1	1 yr., healed
5 ♂	Maxilla, mandible	Swelling of cheek and alveolus	2	3 yr., healed
7 ♀	Maxilla, mandible	Pain, swelling, proptosis	1	4 yr., healed
21 ♀	Maxilla	Alveolar distortion	1	...

Some residual deformity is frequently seen on follow-up x-ray films but no gross distortion is evident. Figure 2 reveals the lesion at the symphysis in the second patient (a fourteen year old boy) preoperatively and eighteen months postoperatively.

Curettage was employed with two additional patients (Table II) but, in addition, the resulting cavities were packed with cancellous bone chips obtained from the iliac crest. These two patients were clinically no different from the others as they presented with their lesions and their chemistries, as in the other five, were normal. The impression has been gained, however, that these latter patients experienced a more rapid and satisfactory filling in of the cavity and tightening of the loose teeth with this technic.

An unusual complication of fibrous dysplasia was seen in the final patient. This thirty-seven year old woman had a lesion in the left zygoma; a biopsy was performed in 1950 and the diagnosis was fibrous dysplasia. She did well for five years and then experienced sudden onset

TABLE II
TWO PATIENTS TREATED BY CURETTAGE AND BONE GRAFT

No. of Patients	Involvement	Symptoms and Signs	No. of Operations	Follow-up
13 ♀	Mandible	Asymptomatic swelling	1	5 yr., healed
10 ♀	Mandible	Asymptomatic expanding	1	6 yr., healed

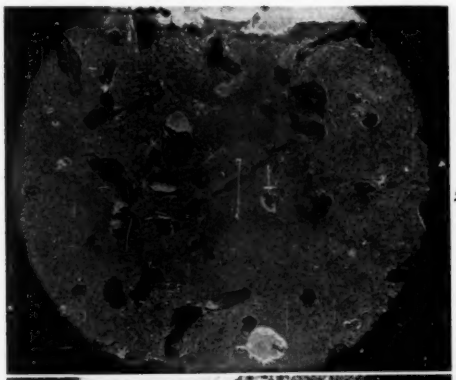
3

4

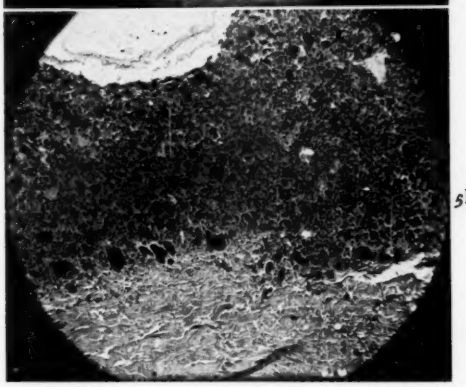
FIG. 3. Sclerotic lesion involving left zygoma in case of osteosarcoma arising in lesion of fibrous dysplasia.

FIG. 4. Fibrous dysplasia in femur and pelvis.

of swelling in the area where the previous biopsy had been performed. X-ray examination showed the lesion in the left zygoma (Fig. 3) to be sclerotic in nature. This was the only patient in the series with generalized bony involvement, for a skeletal survey revealed the typical lesions of fibrous dysplasia in the femur, pelvis and skull. (Fig. 4.) A second biopsy was performed (Fig. 5A) and revealed a lesion similar to that noted previously, typical histologically of fibrous dysplasia. With continued pain and swelling, another biopsy (Fig. 5B) showed an osteogenic sarcoma. Despite surgery and radiation therapy, the lesion was not controlled and the patient died



5A



5B

FIG. 5. A, biopsy of zygoma in Figure 3 showing fibrous dysplasia; B, same patient as in Figure 5, biopsy showing degeneration into sarcoma.

quickly. An autopsy revealed direct cerebral extension of the malignant tumor.

COMMENTS

These cases illustrate many of the important features of fibrous dysplasia of the facial bones. Although this area statistically is less frequently involved than is the remainder of the skeleton [17], dental abnormalities and visibly distorted bony contours give facial involvement an importance out of proportion to its incidence.

Once a diagnosis is made, then surgery is indicated for pain or more commonly increasing facial or dental deformity. As regards a definitive diagnosis, it should be noted that the features of this disease are not entirely exclusive. The roentgenograms frequently merely narrow the diagnostic choices and suggest several alternatives. Normal chemistries provide some aid but the final diagnosis must be made histologically.

The surgery employed should be conservative and appropriate for a benign disorder. With few exceptions, curettage with or without bone grafting would seem to be quite adequate. For most cases resection need not be performed, and curettage and grafting adheres most closely to the basic principles of removal of the lesion along with adequate reconstruction. Even in those cases where recurrent disease requiring surgery is noted, control over the process can be obtained by repeating curettage. One of our patients, prior to referral, had local cystic areas in the mandible removed on five occasions by her dentist, the diagnosis not being made until the last procedure. A more complete curettage resulted in no further progression and healing became evident. Recurrent lesions are common but the indications for operation remain the same as for the primary abnormality. A conservative approach such as this will permit the natural quiescence of this process to become evident and obviate the need for active therapy. It is also understood that an occasional case with extremely rapid growth or marked gross distortion may well require more extensive surgery than has been recommended here.

The case of possible degeneration to malignancy presented represents an extremely unusual complication and its consideration should not alter an over-all conservative approach. Its incidence must be extremely low, only eight cases having been described and documented [*18–23*] from more than several hundred benign cases, this latter figure in all likelihood representing only a fraction of the existing cases.

SUMMARY

1. Eight cases of fibrous dysplasia involving the facial bones have been presented to illustrate some of the features of this disorder.

2. Definitive diagnosis when a biopsy has been performed is recommended.

3. Conservative management is the therapy of choice with observation, or curretage with or without bone chip grafting being indicated.

4. An unusual case involving degeneration to an osteogenic sarcoma is also described.

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A Simplified Technic for Regional Perfusion

REPORT OF ITS USE IN A SERIES OF TWENTY-THREE CASES OF MALIGNANCIES OF THE HEAD AND NECK

FREDERICK M. GOLOMB, M.D., ALDEN B. HALL, M.D., KENNETH R. COX, F.R.C.S., F.R.A.C.S., CHARLES F. SCHETLIN, M.D., STEPHEN L. GUMPORT, M.D. AND JANE C. WRIGHT, M.D.,
New York, New York

From the Department of Surgery, New York University Medical Center, Bellevue Hospital, and University Hospital, New York, New York. This study was supported by grants from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service, Bethesda, Maryland, and by the Shrine Tuberculosis and Cancer Research Foundation.

IN 1957 regional perfusion of human cancers with chemotherapeutic agents was first described [1]. Since then several investigators have reported on their experience with the technic in tumors of the head area [2–4]. The methods employed have been essentially those developed by Creech and his co-workers [5]. These include the use of a heart-lung machine for maintaining an extracorporeal vascular circuit through the tumor-bearing area. In an attempt to overcome some of the technical problems and perhaps increase the versatility of the perfusion concept a simplified technic has been developed. With it the oxygenator, blood for priming, and the heavy equipment are eliminated but the essential principles of perfusion therapy are maintained.

Since December 1958, sixty-one perfusions have been performed for neoplasms of various areas. Twenty-eight have been by the simplified, nonoxygenated technic. (Table 1.) This report concerns the technic and its use in a series of twenty-three perfusions of the head and neck area.

METHOD

The standard perfusion technics as described elsewhere [2–5] were employed for the oxygenated perfusions. A sigmamotor pump and disposable plastic, bubble oxygenator (Abbott or Travenol) were used. The nonoxygenated perfusions as described later were performed in a similar manner using a hand-powered pump.

Equipment. The nonoxygenated perfusion system used is a single unit containing pump, filter and tubing. (Fig. 1.) It is sterile and kept in the operating field, hand operated and disposable. The pump is a plastic bulb equipped with metal ball valves permitting unidirec-

TABLE 1
RESULTS OF ALL PERFUSIONS ACCORDING TO USE OR LACK OF USE OF OXYGEN

Diagnosis	Oxygenated				Nonoxygenated			
	Positive	Negative	Adjuvant	Total	Positive	Negative	Adjuvant	Total
Squamous cell carcinoma	3	2	1	6	9	3	3	15
Adenocarcinoma	5	1	0	6	1	2	0	3
Melanoma	7	0	2	9	2	0	6	8
Sarcoma	6	2	1	9	0	1	1	2
Glioblastoma	2	1	0	3	0	0	0	0
Total	23	6	4	33	12	6	10	28

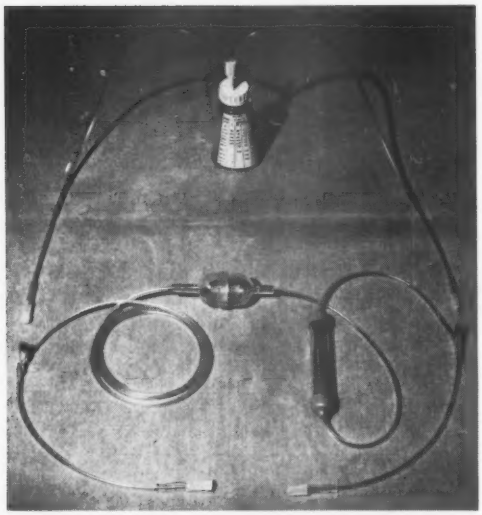

FIG. 1. Pump system for nonoxygenated regional perfusion. The apparatus in the lower part of the illustration is the hand-activated pump, filter and tubing. The vascular catheters or cannulas, not shown, attach to the covered tips at the bottom of the picture. The direction of blood flow is counter-clockwise. The calibrated container and attached tubing are a flow meter which can be plugged into the perfusion circuit at the adapters.

tional flow. The afferent and efferent tubing have adapters for injection of drugs and aspiration of blood samples. A metal sieve filter is interposed on the afferent line. The tubing has adapters for standard needles, cannulas and catheters. Flow rates up to 250 cc./minute can be achieved. A flow meter may be attached to the pump for flow rate determinations during the perfusion.

Technic. General anesthesia is induced and maintained by endotracheal technics. A short, diagonal incision is made along the anterior border of the sternocleidomastoid muscle and the internal jugular vein and external carotid artery are isolated. The artery cannulated depends upon the area to be perfused and may include the external carotid itself or any one or combination of its branches. It is not necessary to give heparin intravenously. The extracorporeal circuit is primed with a mixture of 20 mg. heparin and 100 cc. physiologic saline solution. The internal jugular vein is cannulated below the junction of the common facial vein. It is temporarily occluded above this junction and again below the site of cannulation with umbilical tape tourniquets. A No. 14 or 16 French plastic catheter or No. 13 or 15 gauge blunt-tipped, metal cannula may be used and the prepared and primed tubing is then attached.

The external carotid artery is occluded with a bulldog or Pott's clamp proximal to the site of cannulation. The stump of the thyroid artery may be used or the external carotid artery may be incised and later repaired or ligated. A metal, blunt-tipped cannula with a soldered knob encircling its tip is used. A ligature placed over the vessel keeps the cannula from slipping out of the artery during the perfusion. The arterial tubing is then attached and pumping is performed by quickly and gently squeezing and releasing the bulb. The vascular pressure is determined and sensed by the fingers on the bulb. Flow rates of 50 to 75 cc./minute and low pressures are desirable. If both sides of the neck are to be perfused simultaneously, it is better to use two separate pumps rather than a single pump connected to the two sets of vessels by "Y" tube connections. In using the latter method variations in the resistance within the vessels will favor the flow of perfusate to one side over the other.

Determination of the flow rate may be made during the perfusion as follows: The flow meter and its tubing are filled with heparinized saline or blood. One arm of the meter's tubing is attached to the adapter on the venous line. Hemostats are then placed on both arms of the tubing. At a given signal the clamp on the arm attached to the adapter is released and placed on the venous catheter between the adapter and the patient. The rate of pumping is maintained as before and continued for five, ten, twenty or thirty seconds at the end of which time the clamp on the venous tubing is released and placed back on the meter's tubing. The flow rate in milliliters per minute is then read directly off the calibrated reservoir.

The chemotherapeutic agent is administered through the adapter on the venous line which, being proximal to the pump, prevents streaming. When HN_2 is being used the dose is divided into aliquots given at five minute intervals. Other agents, being less vesicant and of longer duration, may be given as a single injection.

Prior to the injection of the chemotherapeutic agent 2 cc. of 5 per cent fluorescein may be injected into the arterial adapter. The room is darkened and the face illuminated with an

TABLE II

RESULTS OF PERFUSIONS OF MALIGNANCIES OF THE HEAD AND NECK ACCORDING TO CHEMOTHERAPEUTIC AGENT USED

Drug	Objective Tumor Response		Adjuvant Response		Total
	Positive	Negative	No Recurrence	Recurrence	
Dihydro E. 73	7	4	2	1	14
HN_2	2	1	0	1	4
TSPA	1	1	0	0	2
CB 1348	1	0	0	0	1
AT-DNA	0	1	0	0	1
Methotrexate	0	1	0	0	1
Total	11	8	2	2	23

TABLE III

RESULTS OF PERFUSIONS OF MALIGNANCIES OF THE HEAD AND NECK ACCORDING TO DIAGNOSIS

Diagnosis	Objective Tumor Response		Adjuvant Response		Total
	Positive	Negative	No Recurrence	Recurrence	
Squamous cell carcinoma					
Floor of mouth	7	3	1	1	12
Tongue	1	0	1	1	3
Lip	1	2	0	0	3
Larynx	1	0	0	0	1
Melanoma	1	0	0	0	1
Malignant mixed tumor of parotid	0	2	0	0	2
Sarcoma of meninges	0	1	0	0	1
Total	11	8	2	2	23

ultraviolet lamp. The distribution of the fluorescence corresponds with the area perfused. Doing this before injecting the drug permits changes in vessel occlusions necessary to improve upon the localization of the therapy.

Tracer substances may be used to determine the rate of escape of blood from the isolated circuit. RISA® (radioactive iodinated serum albumin) was used in this study. Control samples are drawn from the arm vein and the pump circuit prior to the injection of 50 μc. of RISA into the arterial adapter. Specimens of blood are taken at periodic intervals from the arm and the pump and counted. The leakage rate, as determined in our experience, suggests that in the average case at the end of fifteen minutes sufficient admixture has occurred to justify the termination of the perfusion. As significant isolation does not persist to the termination of the perfusion we have not drained the blood, nor flushed the circuit with fresh blood, to reduce the amount of agent left in the patient.

At the termination of the perfusion the cannulas are removed. The vessels are repaired or ligated. In many instances a polyethylene catheter of small diameter (PE 20) is left in the artery for subsequent intra-arterial infusion of drugs.

Technic During Radical Neck Dissection. If the perfusion is to be performed during the course of a neck dissection as an adjuvant to surgery, the neck dissection is carried out in the routine manner. While the specimen is being swept upward and prior to dividing the external maxillary vessels the external carotid artery and the already divided and usually distended internal jugular vein are cannulated. The perfusion is then performed as described above. At the completion the vessels are repaired or ligated and the dissection proceeds in a routine manner. The indications for tracheostomy are the same as those for the surgical procedure performed.

Drug Selection. Several types of chemotherapeutic agents were studied in this series of cases [6]. (Table II.) Dihydro E-73, an antibiotic similar in structure to actidione, was used in fourteen cases [7]. Three alkylating agents, nitrogen mustard, triethylene thiophosphoramide and Leukeran,® were employed in seven cases. Methotrexate, an antimetabolite, was used in one case, and altered tumor DNA, obtained from the patient's tumor, was used in one case.

RESULTS

Twenty-three head and neck perfusions were performed on twenty-one patients between January 1959 and January 1961. (Table III.) Nineteen were performed for squamous cell carcinoma, of which twelve were of the floor of the mouth, three of the tongue, three of the lower lip and one of the larynx. One patient each with melanoma, malignant mixed tumor of the parotid and sarcoma of the meninges

TABLE IV

RESULTS OF PERFUSIONS OF MALIGNANCIES OF THE HEAD AND NECK ACCORDING TO USE OR LACK OF USE OF OXYGEN

Diagnosis	Oxygenated				Nonoxygenated			
	Positive	Negative	Adjuvant	Total	Positive	Negative	Adjuvant	Total
Squamous cell carcinoma	2	2	1	5	8	3	3	14
Adenocarcinoma	0	2	0	2	0	0	0	0
Melanoma	0	0	0	0	1	0	0	1
Sarcoma	0	0	0	0	0	1	0	1
Total	2	4	1	7	9	4	3	16

were also treated. Of these, four were performed adjuvant to definitive surgical procedures. The remaining patients all had advanced malignant disease considered to be incurable.

Of the technic employed fifteen were unilateral, nine bilateral; seven were oxygenated, sixteen nonoxygenated. (Table IV.)

The results in those cases in which perfusion was performed for palliation are based upon evidence of marked gross tumor necrosis following perfusion. Moderate objective regressions, cessation of tumor growth or relief of pain without marked gross necrosis were not considered positive responses. In ten of fifteen cases of squamous cell carcinoma the response was positive as in one case of melanoma. No response was observed in one case in which perfusion was performed twice for a parotid malignancy and in another for sarcoma of the meninges. (Table III.) Of the drugs used dihydro E-73 was effective in seven of ten cases of squamous cell lesions, HN_2 was effective in two of three (Table V) and Leukeran was effective in the one case in which it was tried. In those cases in which perfusion was performed with an oxygenated circuit, two of six patients responded whereas in those in which the nonoxygenated technic was employed, nine of thirteen patients responded. (Table IV.)

The visible tumor changes became apparent within five days of perfusion and were characterized by a darkening and drying of the surface of the tumor. This was followed by necrosis, liquefaction and slough. Microscopic changes ranging from alterations in nucleocytoplasmic ratio and increased granularity to frank necrosis, were observed. The amount of tumor destruction was occasionally extensive, but in all cases residual tumor has been grossly visible or demonstrable by biopsy at the completion of the separation of slough.

The duration of antitumor effect in this series averaged thirty-four days. The response to dihydro E-73 averaged twenty-one days while the two patients who responded to HN_2 remained free of gross disease for ninety to 120 days before tumor regrowth was noted.

The details of dosage, response and complications are tabulated in Table V.

Four perfusions were performed at the time of extirpative surgery as supplementary or adjunctive therapeutic measures. One patient (Case VIII) with a carcinoma of the floor of the mouth who was perfused with 3.5 mg. dihydro E-73 at the time of a single stage hemimandibulectomy and radical neck dissection is alive and free of recurrent carcinoma twenty months later. Another patient (Case XXIII) with a carcinoma of the tongue was perfused with 56 mg. dihydro E-73 during a single stage hemiglossectomy, partial mandibulectomy and radical neck dissection. There is no recurrence one month later. Another patient (Case XVI) whose large carcinoma of the posterior third of the tongue was incompletely excised during a single stage hemiglossectomy and radical neck dissection was perfused at the time with 28 mg. dihydro E-73. A local recurrence appeared seven months later. The fourth patient, an eighty-four year old man (Case XI) died of a cerebrovascular accident, which occurred the day following a perfusion with 20 mg. HN_2 combined with a hemiglossectomy, hemimandibulectomy and radical neck dissection.

TABLE V

Case No.	Patient, Age (yr.) Sex and C. R. No.	Diagnosis	Type of Perfusion	Drug	Dose (Total) (mg./kg.)	Type of Tumor Response*	Remarks
I	N. C., 66, M, 344	Squamous cell carcinoma of floor of mouth	Unilateral, non-oxygenated	Dihydro E-73	10.4 mg. 0.2 mg./kg.	2	The tumors became black and necrotic in all visible areas; normal tissues not affected; intra-arterial infusions of 10.4 mg. dihydro E-73 for each of 2 days after perfusion; died of pneumonia 3 days later
II	H. K., 74, F, 362	Malignant mixed tumor parotid	Unilateral, oxygenated	Dihydro E-73	7.84 mg. 0.1 mg./kg.	0	Tumor did not respond; patient died of disease 7 mo. later; (see Case v)
III	I. P., 33, F, 363	Melanoma of orbit, right	Unilateral, non-oxygenated	TSPA	45 mg. 1 mg./kg.	2	All tumors in perfused area reduced markedly in size; those outside of perfused zone continued to grow despite poor isolation of drug; radiation-like changes were noted in skin of perfused area; died of pulmonary embolus 8 weeks later
IV	M. K., 75, M, 371	Squamous cell carcinoma of floor of mouth	Bilateral, non-oxygenated	Dihydro E-73	30 mg. 0.6 mg./kg.	2	Marked temporary reduction in tumor size and relief of pain; died of recurrent disease and pneumonia 4 weeks later
V	H. K., 74, F, 362	Malignant mixed tumor parotid	Unilateral. oxygenated	At-DNA	14.6 mg. 0.18 mg./kg.	0	No objective tumor response; died 5 mo. later; (see case II)
VI	A. L., 63, M, 384	Squamous cell carcinoma of floor of mouth	Bilateral, oxygenated	TSPA	75 mg. 1.4 mg./kg.	0	No objective tumor response; died of disease 4 mo. later
VII	J. C., 60, M, 386	Squamous cell carcinoma of larynx	Unilateral, oxygenated	CB 1.348	120 mg. 1.9 mg./kg.	2	A large cervical lymph node on the perfused side became smaller and softer; died of disease 2½ mo. later
VIII	F. K., 72, F, 365	Squamous cell carcinoma of floor of mouth	Bilateral, non-oxygenated	Dihydro E-73	3.5 mg. 0.1 mg./kg.	1	Perfusion combined with a single stage hemimandibulectomy and radical neck dissection without added morbidity; patient is alive and well 20 mo. later
IX	D. T., 8, F, 408	Sarcoma of meninges	Unilateral, non-oxygenated	Methotrexate	45 mg. 1.9 mg./kg.	0	No objective tumor response
X	C. V., 55, M, 413	Squamous cell carcinoma of floor of mouth	Unilateral, oxygenated	HN_2	20 mg. 0.37 mg./kg.	2	Marked reduction in tumor size lasting 3 mo. and alleviation of pain; palliation was remarkable in that the mandible, cervical nodes and skin were involved with tumor; died following infusion therapy 4 mo. later
XI	J. M., 84, M, 422	Squamous cell carcinoma of floor of mouth	Unilateral, oxygenated	HN_2	20 mg. 0.3 mg./kg.	1	Perfusion combined with a single stage hemimandibulectomy, hemiglossectomy and radical neck dissection; he died of a cerebrovascular accident the next day
XII	L. C., 46, M, 421	Squamous cell carcinoma of floor of mouth	Bilateral, oxygenated	HN_2	26.4 mg. 0.4 mg./kg.	0	Technical difficulties necessitated a temporary ligation of the right common carotid during the perfusion; it is believed that HN_2 leaked into the cerebral circulation resulting in a sagittal sinus thrombosis and death 5 days later
XIII	F. S., 74, M, 451	Squamous cell carcinoma of lip	Bilateral, non-oxygenated	Dihydro E-73	14 mg. 0.25 mg./kg.	2	Most of the tumor sloughed away; more response on right side of tumor than left; Y tube may not have distributed drug evenly; subsequent intra-arterial and intratumoral administration of dihydro E-73 ineffective; (see Case XV)
XIV	E. M., 50, M, 467	Squamous cell carcinoma of floor of mouth	Bilateral, non-oxygenated	Dihydro E-73	56 mg. 0.9 mg./kg.	2	Good objective response; most of tumor necrosed; no pain relief; regrowth began 25 days later; died 2½ mo. later following lobotomy for pain
XV	F. S., 74, M, 451	Squamous cell carcinoma of lip	Unilateral, non-oxygenated	Dihydro E-73	56 mg. 1 mg./kg.	0	No response to prior or subsequent infusions of methotrexate; no response to second perfusion with 4 times original dose of dihydro E-73; (see Case XIII)
XVI	J. D., 35, F, 475	Squamous cell carcinoma of tongue	Unilateral, non-oxygenated	Dihydro E-73	28 mg. 0.56 mg./kg.	1	Perfusion combined with single stage hemiglossectomy and radical neck dissection; local recurrence 7 mo. later
XVII	J. M., 64, M, 496	Squamous cell carcinoma of floor of mouth	Bilateral, non-oxygenated	Dihydro E-73	98 mg. 1.7 mg./kg.	0	Patient had an uneventful and satisfactory perfusion; the next morning when his tracheostomy tube was being changed he experienced a cardiac arrest and died
XVIII	N. B., 61, M, 511	Squamous cell carcinoma of lip	Unilateral, non-oxygenated	Dihydro E-73	98 mg. 1.6 mg./kg.	0	Perfusion was uneventful; patient was alert, cooperative and asymptomatic the next a.m.; while being turned in bed syncope and vascular collapse developed and he died 24 hours later; (autopsy refused)

*Tumor response: 2, objective tumor regression; 1, intermediate response (adjuvant to definitive surgery); 0, no objective tumor regression.

TABLE V (*Continued*)

Case No.	Patient, Age (yr.) Sex and C. R. No.	Diagnosis	Type of Perfusion	Drug	Dose (Total)	Type of Tumor Response	Remarks
XIX	J. S., 55, M, 510	Squamous cell carcinoma of tongue	Bilateral, non-oxygenated	Dihydro E-73	54 mg. 1.1 mg./kg.	2	Necrosis and shrinking of tumor noted; infusion of dihydro E-73 was begun on 2nd postoperative day, did well until 8th postoperative day when he suddenly and unexpectedly died. No cause was found at autopsy
XX	W. Y., 53, M, 525	Squamous cell carcinoma of floor of mouth	Unilateral, non-oxygenated	Dihydro E-73	54 mg. 1 mg./kg.	2	Response was good, but regrowth began 3 weeks after perfusion
XXI	P. D., 53, M, 512	Squamous cell carcinoma of floor of mouth	Unilateral, non-oxygenated	HN_2	28 mg. 0.5 mg./kg.	2	Complete necrosis of all visible tumor; response was associated with necrosis and edema of face, cheek, neck and paralysis of seventh nerve; recurrence noted 5 mo. later
XXII	J. V., 46, M, 552	Squamous cell carcinoma of mouth	Unilateral, non-oxygenated	Dihydro E-73	56 mg. 1 mg./kg.	2	Partial necrosis of large tumor resulted; regrowth noted 4 weeks later
XXIII	A. M., 66, M, 619	Squamous cell carcinoma of tongue	Unilateral, non-oxygenated	Dihydro E-73	56 mg. 0.7 mg./kg.	1	Perfused at time of hemiglossectomy, partial mandibulectomy and radical neck dissection; no recurrence 1 mo. later

COMMENTS

The clinical results in this series of cases must be interpreted according to the disease treated and the drugs used. Most of the patients with squamous cell carcinomas were treated with dihydro E-73, a new drug undergoing its initial clinical trial by perfusion [8]. While three of ten patients did not respond to treatment, two of them died in the immediate postoperative period due to excessive doses and the third had responded well to a prior perfusion with the same drug. Nevertheless, the duration of effect was shorter with dihydro E-73 than with nitrogen mustard. As its toxic manifestations do not include local tissue necrosis or bone marrow depression, it may prove to be a useful drug in combination with one of the alkylating agents. The negative responses to the patients treated with altered tumor DNA and methotrexate can be attributed to the choice of agents used.

While it is generally accepted that the beneficial effects of regional perfusion depend to a large extent upon the degree of isolation achieved, experience with perfusions of the head and neck suggest that complete or nearly complete isolation is not necessary to achieve results. The degree of isolation ranges from less than 25 per cent [4] to as high as 85 per cent [9]. The significance of these observations with radioactive tagged albumin may not be directly applicable to the rate of escape of the chemotherapeutic agents being perfused. For, despite the apparently high rate of leakage intensely localized effects are noted within the perfused zone when alkylating agents are used.

The clinical response in some patients with poorly isolated tumors may also be due to the high drug concentrations achieved, albeit for brief periods. The rate of drug leakage from the isolated circuit in a variety of area perfusions is illustrated in Figure 2. These curves are derived from our studies of the escape of RISA from these circuits. It appears that rather high concentrations are attainable in the head area, despite a rapid rate of drug leakage. This high initial drug concentration may contribute to the effects achieved.

The use of the nonoxygenated circuit is predicated upon the limited importance of an oxygenator in a partially isolated area. In regional perfusions, such as the head and neck, in which isolation is poor, the increase in oxygen tension with the oxygenators currently employed is only slight. Furthermore, the necessity of oxygenating the blood perfusate is in doubt. Its use is based upon the enhanced effect of ionizing irradiation attained by increasing the tissue oxygen tension and the assumption that a similar enhancement may occur with chemotherapeutic drugs. Studies with transplanted mouse tumors treated with HN_2 in the presence of increased tissue oxygen tension tend to support this contention [10]. But, Ausman and Aust [11] using the

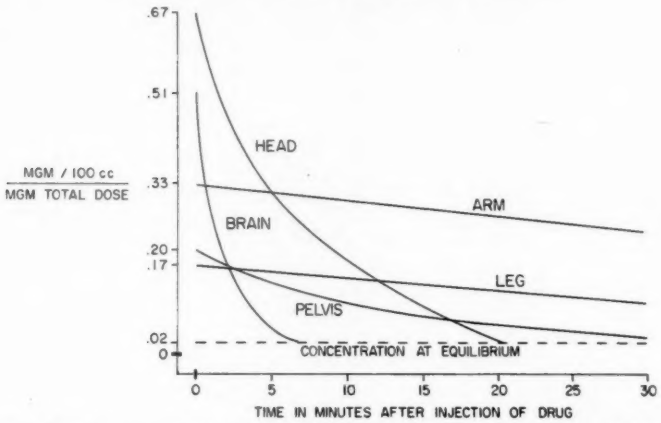

FIG. 2. These concentration curves are based upon the rate of leakage of RISA from the isolated circuits during perfusion. The curves are averages of our experience in perfusions of the head (unilateral and bilateral external carotid-internal jugular circuits), brain (unilateral internal carotid-internal jugular circuits), pelvis, arm and leg. The drug concentrations illustrated are for a hypothetic patient with a whole blood volume of 5 L. The concentration at equilibrium is that which would be achieved if the quantity of drug used in the perfusate had been given to the patient intravenously, or if complete mixing between the isolated and systemic circulations takes place. With the exception of nitrogen mustard, actinomycin D and phenylalanine mustard which are damaging to blood vessels in high concentrations, the doses employed are the maximum which it is estimated the patient could receive systemically, at a single instance, without producing severe systemic toxicity. The concentration of drug delivered to a tumor-bearing area at the beginning of a perfusion is in the order of ten times for the pelvis, eight times for the leg, ten times for the arm, twenty-five times for the brain and thirty-three times for the head as could be safely delivered by any single systemic dose.

perfused hind limb of a dog noted greater uptake of nitrogen mustard by the experimental leg maintained at 70 to 85 per cent oxygen saturation than the control leg at 100 per cent oxygen saturation.

The enhancement of antitumor effect by an oxygenated circuit for perfusions of the head has not been supported by the results of this study. In 33 per cent of the oxygenated cases a positive antitumor response was achieved while in the nonoxygenated series 70 per cent responded.

The brief duration of perfusions of the head and neck and the high degree of collateral blood supply make the use of an oxygenated circuit unnecessary to maintain tissue viability.

There is a tendency among some surgical chemotherapists to abandon perfusion in favor of infusion therapy for tumors of the head and neck [*4,12*]. One of the motivating factors is the duration and complexity of standard perfusion procedures. The nonoxygenated perfusion eliminates several of the factors which tend to complicate the procedure principally: the services of a trained professional and technical team, blood for priming and the complex of pump, oxygenator, heat exchanger and lengths of sterile tubing and connectors. This simplified approach maintains the important primary principle of regional perfusion which is recirculation of a high concentration of drug through the tumor-bearing area. It permits the use of the majority of effective chemotherapeutic agents which, having no antidotes, would not be suitable for infusion therapy. As the dissection for this perfusion is essentially the same as for the installation of indwelling arterial catheters, there is very little extra surgery added. While we have not made it our usual practice to follow perfusion with infusion therapy, in order to fully evaluate the effects of the former method, it seems logical that to achieve the best results from chemotherapy a combination of modalities might be

used. Following the perfusion with an alkylating agent or antibiotic, fine catheters can be left in the appropriate vessels for the subsequent infusion treatment with antimetabolite-metabolite therapy described by Sullivan [*13*].

The concomitant use of general hypothermia and hyperthermia in the isolated circuit as advocated by Singleton [*14*] in perfusion of the abdominal organs might lend itself to perfusions of the head and neck area. With the use of rapid acting alkylating agents systemic toxicity can be reduced; however, the limiting factor of dosage in this area is usually local tissue toxicity.

CONCLUSIONS

A simplified, nonoxygenated method for performing regional perfusions and its applicability in palliative and adjuvant perfusions of the head and neck area is presented.

The results of a clinical experience with twenty-three cases of perfusion therapy for malignancies of the head and neck is presented.

Several chemotherapeutic agents are effective in obtaining selective tumor necrosis in this area. The drugs found to be of value in this series are: dihydro E-73, nitrogen mustard, triethylene thiophosphoramide and Leukeran.

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Comparative Incidence of Stones in the Common Duct in Acute and Chronic Cholecystitis (and Their Relationship to the Number of Calculi in the Gallbladder)

ALEX E. PEARCE, M.D., *Philadelphia, Pennsylvania*

From the Department of Surgery, Hahnemann Medical College and Hospital, Philadelphia, Pennsylvania.

MUCH attention has been focused on the comparative frequency of solitary and multiple stones in the gallbladder in acute and chronic cholecystitis. In 484 patients with acute cholecystitis, Carveth, Priestly and Gage [1] found 119 (24.6 per cent) with solitary stones and 365 (75.4 per cent) with multiple calculi. In a review of 416 patients with chronic cholecystitis they found seventy-seven (18.5 per cent) with solitary stones and 339 (81.5 per cent) with multiple calculi. Mechling and Watson [2] found solitary gallstones in eighty-two (21.2 per cent) of 387 patients with cholelithiasis, fifteen (18.3 per cent) of which were associated with acute cholecystitis. The incidence of stones in the common duct was 6.9 per cent (twenty-one patients) in the patients with multiple calculi and 6.1 per cent (5 patients) in those with a solitary calculus. Each of the latter five patients had the single stone in the common duct without calculi in the gallbladder.

A more important consideration is that patients with acute cholecystitis are more apt to have associated stones in the common duct than those with chronic cholecystitis. In a series [3] of 162 patients with acute cholecystitis operated on by me from January 1950 to December 1958, 159 had calculi in the gallbladder. (Table I.) Of these, thirty-seven (23.3 per cent) had a solitary calculus, ninety-eight (61.6 per cent) had multiple stones and twenty-four (15.1 per cent) had multiple stones in the gallbladder and in the common duct. In a concomitant series of 337 patients with chronic cholecystitis, fifty-five (16.3 per cent) had single stones, 247 (73.3 per cent) multiple stones and thirty-five (10.4 per cent) had multiple calculi in the gallbladder and common duct. There were no stones in the common duct in any of the patients who had a solitary calculus in the gallbladder. In this series, therefore, the incidence of solitary stone in acute cholecystitis was one and a half times that seen in patients with chronic disease; further, the incidence of stones in the common duct in patients with acute disease was one and a half

TABLE I

INCIDENCE OF CALCULI IN COMMON DUCT IN ALL PATIENTS WITH ACUTE CALCULUS CHOLECYSTITIS AND IN ALL PATIENTS WITH CHRONIC CALCULUS CHOLECYSTITIS

	Single		Multiple		Stones in Common Duct	
	No.	%	No.	%	No.	%
Patients with acute calculus cholecystitis (159)	37	23.3	98	61.6	24	15.1
Patients with chronic calculus cholecystitis (337)	55	16.3	247	73.3	35	10.4

TABLE II

INCIDENCE OF CALCULI IN COMMON DUCT IN PATIENTS WITH ACUTE CHOLECYSTITIS AND IN PATIENTS WITH CHRONIC CHOLECYSTITIS IN WHOM MULTIPLE CALCULI OF GALLBLADDER ARE PRESENT

	Calculi in Common Duct		Ratio
	No.	%	
Patients with acute cholecystitis (122)	24	19.7	1.6:1
Patients with chronic cholecystitis (282)	35	12.4	

TABLE III

ACUTE CHOLECYSTITIS, OPERATIVE PROCEDURE

Procedure	Operations	
	No.	%
Cholecystectomy—total	159	98.2
Cholecystectomy alone 94 (58.0%)		
with exploration of common duct 23 (14.2%)		
with exploration of common duct and operative cholangiogram 21 (13.0%)		
with operative cholangiogram 21 (13.0%)		
Partial cholecystectomy with cholecystostomy (bad risk cardiac)	1	0.6
Cholecystostomy (associated carcinoma of gallbladder)	1	0.6
Jejunotomy with extraction of calculi	1	0.6
	162	100.0

times that seen in patients with chronic inflammation. If these data of multiple stones and calculi in the common duct are combined, the patients with acute cholecystitis and multiple calculi in the gallbladder have 60 per cent more chance of having calculi in the common duct than do those with chronic cholecystitis and multiple gallbladder stones. (Table II.)

Zollinger and Cutler [4] found twenty-three patients (14.9 per cent) with stones in the common duct in a series of 156 patients with acute cholecystitis; fifty-seven were subjected to choledochostomy. Glenn [5] described 697 patients with acute cholecystitis: 618 (88.4 per cent) treated by cholecystectomy and eighty-one (11.6 per cent) by cholecystotostomy; 61 (8.8 per cent) had an associated choledochotomy. In 268 patients fifty years of age and over, thirty (11.2 per cent) underwent exploration of the common duct; stones were found in twenty-one (7.8 per cent). In 429 patients under fifty years of age, exploration of the common duct was performed in thirty-one (7.2 per cent); stones were recovered in nineteen (4.4 per cent of the total). Buxton, Ray and Coller [6] reported seventy-three operations in 109 patients. Nine of forty-two who had cholecystectomies were also subjected to choledochotomies; four had calculi in the common duct (5.5 per cent of the total). Holden, Cebul and Laughry [7] performed an exploration of the common duct in fifty-seven (18 per cent) of 315 patients undergoing operations; stones were found in twenty-two (6.9 per cent of the total). Dunphy and Ross [8] recovered stones from the common duct in twenty-eight of fifty-six explorations of 134 total operations for acute cholecystitis; this constituted 20.7 per cent of the total cases. Colcock and Liddle [9] reported on 1,077 patients with cholecystitis subjected to surgery. Of these 948 had stones. Exploration of the common duct was carried out in 389 (36.1 per cent of the total of 1,077); calculi in the duct were discovered in 138 (35.5 per cent of the 389 and 14.9 per cent of the 1,077). He reviewed previous data from the Lahey Clinic [10] in which exploration of the common duct was carried out in 45.7 per cent of cases, in 36.7 per cent of which stones were present (16.8 per cent of the total 1,356 cases). Although the rate of exploration had decreased 10 per cent, the incidence of stones in the common duct was only slightly lower. The most recent figures at the Lahey Clinic indicate that the rate of exploration is the same (36.7 per cent) but that the figure for stones found in those undergoing the procedure has dropped slightly (28.5 per cent). In an eight year period Colcock [11] reported on 2,460 patients operated on for disease of the biliary tract in 13.3 per cent of whom stones were found in the common duct. At present at the Lahey Clinic, slightly more than a third of the patients undergo explorations of the common duct and stones are found in slightly less than a third of those undergoing exploration. Although Colcock did not give the number of patients who had acute cholecystitis, he

said stones were found in the common duct in 24 per cent of patients with acute or subacute disease, or three times as frequently as in those with chronic cholecystitis. Smith et al. [12] said the problem of retained stones is primarily related to the patient who has or has had stones in the common bile duct. They reported 0.8 per cent retained stones in the common duct after cholecystectomy alone, 1 per cent after exploration of the common duct when stones were not found and 11 per cent when stones had been removed previously.

It has been my practice to open the gallbladder routinely in the operating room to determine the presence of multiple stones. Often concomitant small stones cannot be palpated through the intact gallbladder wall, especially when one or more large calculi are present. Routine operative cholangiography has also been effective in demonstrating or ruling out stones in the common duct. It is surprising how easily injection of the common duct with opaque material can be made after an acutely inflamed gallbladder has been decompressed or removed. The ductal area often shows little inflammatory reaction. My preference is for direct injection into the common duct with a No. 25 hypodermic needle which is bent to a 60 to 90 degree curve. This method is technically easier and eliminates the introduction of air bubbles into the duct. In 162 operative procedures for acute cholecystitis, information concerning the common duct was obtained in 40 per cent of the cases. (Table III.) Of 159 patients subjected to cholecystectomy, twenty-three (14 per cent) underwent an associated exploration of the common duct, twenty-one (13 per cent) also underwent exploration of the common duct with operative cholangiogram and twenty-one (13 per cent) underwent operative cholangiography alone. In recent years, operative cholangiography has been performed routinely. This has produced a reduction in the number of explorations of the common duct.

SUMMARY

Calculi in the common duct occur 60 per cent more often in patients with acute cholecystitis and multiple calculi than in patients with chronic cholecystitis and multiple calculi. Of 122 patients with acute cholecystitis and multiple calculi in the gallbladder, twenty-four (19.7 per cent) had associated stones in the common duct. Of 282 patients with chronic cholecystitis and multiple calculi in the gallbladder, thirty-five (12.4 per cent) had calculi in the common duct. Therefore, the status of the common duct is more important, and its exploration by incision or by operative cholangiography or by both is more essential in patients with acute cholecystitis than in patients with chronic cholecystitis. No patient with a solitary calculus in the gallbladder (thirty-seven or 23.3 per cent of patients with acute cholecystitis and fifty-five or 16.3 per cent of those with chronic cholecystitis) had associated stones in the common duct.

Calculi in the common duct occur more often in patients with acute calculus cholecystitis than in patients with chronic calculus cholecystitis. When multiple calculi exist in the gallbladder, the difference is even more striking.

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Coccygectomy

KENNETH F. SPENCE, JR., M.D., *Bethesda, Maryland*

From the Department of Orthopedics, U. S. Naval Hospital, Bethesda, Maryland. The opinions and views expressed are those of the author and are not to be construed as official or necessarily reflecting those of the Medical Department of the U. S. Navy or the Naval Service at large.

COCCYGECTOMY is widely considered to be ineffective in relieving the symptoms of coccygodynia; many doctors condemn it. During the period 1947 to 1959, twenty patients with coccygodynia underwent coccygectomy at the U. S. Naval Hospital, Bethesda, Maryland. An analysis of the results following this procedure reveals that the operation does not deserve such condemnation. In fact, it often proved to be an effective remedy in relieving persistent and disabling symptoms which did not respond to conservative measures. A review of the literature dealing with this problem will be briefly presented with an analysis of these twenty cases.

Many theories have been offered as to the causes of coccygodynia. These range from the theory that it is primarily a neurotic symptom, to the belief that there are few or none of the usual manifestations associated with functional disturbances present in these patients. The symptom complex seen in this condition has been attributed to direct trauma with resulting fracture, sprain or dislocation of the sacrococcygeal joint, neuritis, neuralgia, arthritis, anorectal disease or any inflammatory process which might cause reflex spasm of the pelvic muscles, poor posture, neoplasm or referred pain from lumbosacral disease [*1,2,4–7*]. Any one, or a combination of these entities may cause coccygodynia.

The majority of patients with complaints of coccygodynia can be cured by conservative measures. These include sedatives, muscle relaxants, rectal suppositories, hot and cold applications, electrotherapy, massage of the coccyx, strapping of the buttocks, postural training, the use of a rubber ring or pillow, the use of a firm corset or girdle, hot baths and laxatives [*1–6,7*]. Local injections with xylocaine and/or hydrocortisone may be used after establishing that the pain is local in origin; these drugs are most effective if the pain can be reproduced on movement of the coccyx [*5*]. When these conservative measures fail, coccygectomy should be considered [*3,5,6*].

The use of coccygectomy has fluctuated through the years; at times being condemned and at other times being enthusiastically endorsed. The first recorded coccygectomy was performed in 1726 by Petit for what was probably tuberculosis of the coccyx. In 1840 Blundell advised resection of the coccyx for relief of pain of undetermined origin in that area [*3*]. In 1859 Simpson coined the term coccygodynia, thus grouping all types of persistent pain in the region of the coccyx under one heading. In the late 1800's and in the early part of this century, coccygectomy became a fad, and for many years it was a common operation, being used indiscriminately [*5*]. Such indiscriminate use led to many failures; thus, surgery of the coccyx fell into disfavor. This in turn brought about a revival of interest in conservative methods of treatment.

In 1937 Duncan reported a series of 278 patients with coccygodynia. Of this group thirty patients had operative resection of the coccyx. Of these, 74 per cent were completely relieved of coccygeal pain, 9 per cent had partial relief, and 17 per cent were not improved [*3*].

In 1957 Powers [*5*] reported a series of twenty-seven patients who had had a coccygectomy. He classified the results of twenty-one of these operations as excellent. He was unable to correlate the history and physical findings with the benefits received from coccygectomy in his series.

We recently reviewed the records of those patients having had a coccygectomy performed

TABLE I
EFFECT OF COCCYGECTOMY

Effect	Patients	
	No.	%
Complete relief	7	39
Marked improvement	7	39
Slight improvement	2	11
No relief	0	0
Worse than before surgery	2	11
Total	18	100

TABLE II
LOW BACK PAIN IN ASSOCIATION WITH COCCYGEAL PAIN

Pain	Patients	
	No.	%
None	11	61
Yes, and relieved along with coccygeal pain after surgery	3	17
Yes, and still present intermittently	4	22
Total	18	100

at the U. S. Naval Hospital, Bethesda, Maryland, between the years 1947 and 1959; a total of twenty-two patients who underwent excision of the coccyx for various reasons. Of these twenty-two, one was dead and one was lost to follow-up examination. A questionnaire asking for pertinent information was sent to and received from the remaining twenty patients. In addition, each chart was closely perused in an attempt to correlate the details of the history, onset of symptoms and physical findings with the success or failure of the procedure. In two patients the coccygectomy was performed incidentally in the care of shrapnel and gunshot wounds. Both of these patients are now asymptomatic. However, since we are primarily interested in the value of coccygectomy in the typical patient with coccygodynia, these two cases are not included in the statistical analysis.

Each patient was asked to furnish his own estimate of the effect of the coccygectomy on his coccygeal pain. Table I reveals that fourteen (78 per cent) replied that they either had complete relief or marked improvement in their symptoms. One patient reported that he was worse than before surgery and that subsequent to the coccygectomy performed at this hospital, another operative procedure with further excision of the coccyx was performed and following that operation he experienced considerable relief of his symptoms.

Table II shows that seven (39 per cent) patients had low back pain in association with their coccygeal symptoms. In three of these patients the symptoms in both sites were relieved postoperatively. In four patients the back pain is still present intermittently, but these four stated that there was marked improvement in their coccygeal pain.

Most series reveal that very often a history of injury is related to the onset of coccygodynia. Table III reveals that in this series, eight (44.5 per cent) patients had an injury associated with the onset of their symptoms. Two patients noted the onset of their symptoms followed a spinal fusion. Both of these patients had complete relief from pain after coccygectomy.

TABLE III
INJURY ASSOCIATED WITH ONSET OF SYMPTOMS

Injury	Patients	
	No.	%
No injury	8	44.5
Previous injury	8	44.5
Onset following spinal fusion	2	11.0
	18	100

The patients were asked if they had received conservative therapy prior to surgery. Only thirteen (72 per cent) replied that they had. However, a review of the patient's charts revealed that some form of conservative therapy had been used prior to surgery on all the patients. The types of conservative therapy included the usual treatments from hot packs to injections.

We were interested in evaluating the time required to obtain maximum benefits following

TABLE IV
INFECTION IN COCCYGEAL AREA BEFORE SURGERY

Infections	Patients	
	No.	%
No infection	14	78
Infection present (cleared after surgery)	2	11
Infection present (did not clear after surgery)	2	11
Total	18	100

TABLE V
DURATION OF SYMPTOMS BEFORE SURGERY

Range	1 month to 15 years
Average	2.6 years (including patient with 15 year history of symptoms)
	1.8 years (excluding patient with 15 year history of symptoms)

TABLE VI
PERCENTAGE OF MALES AND FEMALES HAVING COCCYGEAL SYMPTOMS

Sex	Patients	
	No.	%
Men	6	33
Women	12	67
Total	18	100

surgery. The interval ranged from immediate post operative relief to two years before maximum benefits were obtained, an average of three months. Four patients had complete relief of their symptoms immediately.

Table IV reveals that fourteen (78 per cent) of these patients reported that there had been no infection or anorectal disease present in association with their coccygeal symptoms. Two of the remaining four patients stated that they had pilonidal cysts prior to surgery, which are still present and draining intermittently; in spite of this, they had marked improvement in their coccygeal symptoms.

Table V reveals that the duration of symptoms prior to surgery ranged from one month to fifteen years with an average of two years. There seemed to be no correlation between the duration of symptoms and the relief of pain from the surgery.

Table VI reveals that of these patients, six were men and twelve were women. Their age at the time of surgery ranged from twenty-one to forty-nine years, an average of 32.8 years. The duration of follow-up examinations ranged from one to twelve and a half years, an average of 3.9 years.

COMMENTS

The record of each patient was closely examined in an effort to find a common symptom which might indicate the patients who would benefit by surgery and from those who would not. It was impossible to make any definite correlation. However, it is of interest that most of the patients who had complete relief or marked improvement of their symptoms from coccygectomy had had an injection of a local anesthetic into the coccygeal area with temporary relief of their symptoms.

The report on rectal examination of most of these patients was essentially the same, with anterior angulation of the coccyx, pain to palpation of the sacrococcygeal ligaments and pain on movement of the sacrococcygeal joint.

Duncan [3], in 1937, reviewed the roentgenograms of the pelvis of 262 patients with complaints of coccygodynia and of 200 patients without coccygodynia. He concluded that, except when a fracture, dislocation or osteoarthritis was present, there was no common variation in bone structure associated with a painful coccyx. The roentgenograms of all the patients were not available and therefore an analysis cannot be given in this report.

We realize that all factors which might influence the patient's response to surgery have not been considered. These factors would include change of environment, change in working conditions and change in general health.

SUMMARY

A brief review of the theories of causes and the methods of conservative treatment for coccygodynia are presented.

The records of eighteen cases of coccygectomy for coccygodynia performed at the U. S.

Naval Hospital, Bethesda, Maryland, between the years 1947 and 1959 were reviewed.

Fourteen (78 per cent) patients had either complete relief or marked improvement of their symptoms.

An effort was made to correlate the patient's medical history and physical findings with the benefits received from the coccygectomy. No common symptom for correlation was found.

It appears in reviewing this series and the series recently published by others, that universal condemnation of performing a coccygectomy on a patient with coccygodynia is not warranted.

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Rotation of Esophageal and Pharyngeal Flaps for Reconstruction of the Cervical Esophagus

FRANK C. MARCHETTA, M.D., F.A.C.S., KUMAO SAKO, M.D. AND PATRICK J. CREEDON, M.D.,
Buffalo, New York

From the Department of Surgery, Head and Neck Service, Roswell Park Memorial Institute, Buffalo, New York. Supported in part by American Cancer Society Grant T-129-T.

IN SOME INSTANCES the removal of a tumor requires resection of a complete segment of pharynx and cervical esophagus. Reconstruction of the defect is necessary to re-establish a functional swallowing organ.

There are two accepted methods of reconstruction of the cervical esophagus. The first utilizes split thickness skin [1,2] which is sutured over a prosthesis shaped to the size of the resected segment of esophagus and pharynx. In time the skin graft adheres to the normal adjacent tissue and the prosthesis is removed through the mouth leaving a tubular cavity lined by skin. The second method utilizes skin flaps from the neck or anterior chest wall to reconstruct the defect between the base of the tongue and the esophagus [3–5].

The present experiments were carried out to determine the feasibility of rotating full thickness flaps of the esophageal and/or pharyngeal wall to bridge the defect created by resection of a complete segment of cervical esophagus.

METHOD

Surgery under general anesthesia was performed upon nineteen adult dogs. The neck was entered through a vertical midline incision. A segment of cervical esophagus 4 to 5 cm. in length was completely resected. In fourteen animals, a full thickness flap, 4 by 1.5 cm., of esophageal wall was rotated upward to bridge the defect. The distal free edge of the flap was sutured to the cut end of the pharynx. In five animals, a 2.5 by 1.5 cm. flap was rotated both from the distal esophagus upward and from the proximal esophagus and pharynx downward. The edges of the rotated flaps were sutured to each other, resulting in a complete bridge of tissue, 1.5 cm. in width, connecting the pharynx above and the esophagus below. This bridge of tissue consisted of mucosa, muscularis mucosa and muscularis and was left open. No attempt was made to tube this strip nor was a prosthesis or nasogastric tube used to aid in tubulation.

1A 1B 1C

FIG. 1. A, segment of cervical esophagus dissected free and ready for resection. B, segment of cervical esophagus has been resected. C, a flap has been rotated from both the esophageal end and the pharyngeal end of the transected esophagus. The edges of the flap are sutured to each other to bridge the defect.

TABLE 1

ROTATION OF ESOPHAGEAL AND PHARYNGEAL FLAPS FOR RECONSTRUCTION OF CERVICAL ESOPHAGUS

Dog No.	Length of Resected Segment (cm.)	Length of Rotated Flap (cm.)		Days Alive (postoperatively)	Remarks	Tubulation	Ability to Swallow
		Esophageal	Pharyngeal				
527	4	4 × 1.5	...	1	Died	No	...
323	4	4 × 1.5	...	4	Died	No	...
209	5	5 × 1.5	...	11	Died	No	...
318	5	5 × 1.5	...	13	Died	No	...
339	4	4 × 1.5	...	14	Died	No	...
577	4	2 × 1.5	2 × 1.5	19	Died	No	...
329	3	3 × 1.5	...	24	Died	Partial	Fair
483	4	4 × 1.5	...	26	Sacrificed	Complete	Good
360	3	3 × 1.5	...	30	Died	Partial	Fair
484	3	3 × 1.5	...	40	Died	Complete	Stricture
651	4	2 × 1.5	2 × 1.5	50	Sacrificed	Complete	Good
356	2	3 × 1.5	...	53	Sacrificed	Complete	Good
509	4	4 × 1.5	...	60	Died	Complete	Stricture
409	3	3 × 1.5	...	61	Died	Complete	Stricture
528	4	4 × 1.5	...	68	Died	Complete	Good
612	4	2 × 1.5	2 × 1.5	81	Died	Complete	Good
559	4	2 × 1.5	2 × 1.5	100	Sacrificed	Complete	Good
564	4	2 × 1.5	2 × 1.5	223	Sacrificed	Complete	Good
539	4	4 × 1.5		275	Sacrificed	Complete	Good

(Fig. 1.) A Penrose drain was used to drain secretions and saliva from the operative field. A gastrostomy was performed for feeding.

Postoperatively the dogs received penicillin and streptomycin for five days and subcutaneous fluids for two days. Gastrostomy feedings were started on the third day, first using clear liquids, later dog food with bouillon thinned out with water.

RESULTS

Some difficulty was encountered in maintaining adequate nutrition in these animals during the postoperative period despite gastrostomy. Leakage around the gastrostomy tube or leakage as a result of the animal chewing off the tip of the gastrostomy tube resulted in large electrolyte loss and inanition. Animals were offered water as early as the fourteenth day at which time the neck wound (in the group of successful results) was clinically healed. Complete tubulation demonstrated both by x-ray examination and autopsy occurred as early as the twenty-sixth day.

More complete details of findings in individual animals were these:

Dog No. 527 died postoperatively.

Dogs No. 323, 209, 318, 339 and 577 died within nineteen days of the surgery. In each instance, there was breakdown of the suture line with retraction of the anastomotic edges and subsequent fibrosis and obstruction at the operative site. Tubulation had not occurred in any of these animals. Death was due to inanition, aspiration of saliva and food and pneumonia.

Dogs No. 329 and 360 died on the twenty-fourth and thirtieth postoperative day, respectively. In both instances, partial or incomplete tubulation had occurred. It was interesting to note that despite a persistent esophageal cutaneous fistula these animals were able to swallow water with fair success.

Dogs No. 383, 509 and 409 died on the fortieth, sixtieth and sixty-first postoperative day. Although tubulation had occurred, each of these animals had developed a marked stricture at the site of anastomosis. The stricture interfered with swallowing, resulting in inanition,

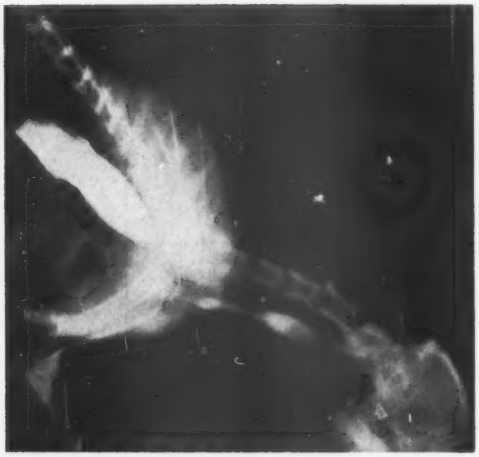

FIG. 2. Barium swallow in dog one hundred seventy-six days after surgery.

FIG. 3. Gross specimen, dog No. 483, sacrificed twenty-six days after surgery. Tubulation was complete. Half-inch rubber tubing was passed through the lumen to demonstrate the patency and caliber of the new esophagus.

aspiration of saliva, bronchopneumonia and death.

The remaining eight dogs (No. 483, 651, 356, 528, 612, 559, and 564 539) all showed complete tubulation and demonstrated good swallowing function. Esophagrams were obtained by feeding the animals a barium meal mixed with bouillon. In each instance, the barium passed readily through the esophagus and into the stomach. There was evident narrowing throughout the operative segment but no evidence of stricture, obstruction or fistula. (Table 1, Fig. 2.)

The operative areas were studied grossly and histologically at twenty-six, fifty, fifty-three, sixty-eight, eighty-one, one hundred, two hundred twenty-three, and two hundred seventy-five days. The operative segments were visibly narrower in diameter than the distal normal esophagus. There was, however, no evidence of abscess, sinus tract or fistula formation in these animals. (Fig. 3.) At twenty-six days, the tubulated segment was composed grossly of two distinct components. Approximately 50 per cent of the circumference of the segment was thick, pliable and distensible and was readily identified as the original strip of esophageal and pharyngeal wall which had been initially rotated. The remaining 50 per cent of the tubulated segment was composed of thin, fibrous, transparent tissue which did not stretch. In eighty-one days the fibrous portion of the wall had diminished considerably in width and at two hundred seventy-five days the fibrous portion was grossly almost absent.

Histologically, the lumens of the tubulated areas were lined by stratified squamous epithelium. The original strip of pharyngeal esophageal wall was readily recognized and was composed of mucosa, muscularis mucosa and muscle layers. The remainder of the circumference was composed of an inner layer of stratified squamous epithelium and an outer layer of fibrous tissue. This corresponded to the thin fibrous layer described under gross findings.

Histologic sections showed that, at the end of twenty-six days, approximately half the tubulated area was composed of all layers and represented the original rotated flaps. The remaining circumferential segment of the tube was composed of fibrous tissue over an inner layer of stratified squamous epithelium. (Fig. 4.) One hundred days after surgery 80 per cent of the tubulated area contained all layers, whereas only 20 per cent was composed of an inner layer of stratified squamous epithelium and an outer fibrous layer. (Fig. 5.) Two hundred twenty-three days after surgery the fibrous segment was less than 5 per cent of the circumference of the tubulated area. (Fig. 6.)

In fourteen of the animals a single flap (4 to 5 cm. in length in the relaxed state) was rotated from the distal esophagus and anastomosed to the proximal cut end of the esophagus. Of these, four showed complete tubulation with good swallowing function, three showed complete tubulation with stricture at the line of anastomosis, two showed partial tubulation and five showed no tubulation.

In five animals, two shorter flaps (2 cm. in

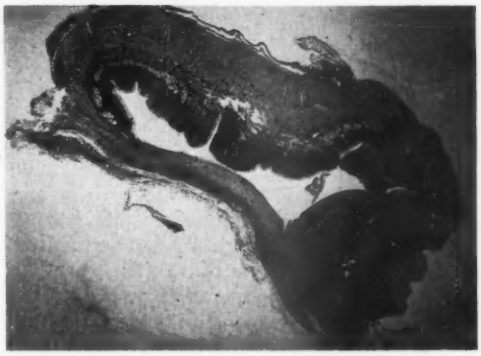

FIG. 4. Histologic sections of specimen twenty-six days after surgery, dog No. 483. The fibrous segment forms approximately 50 per cent of the circumference of the tube.

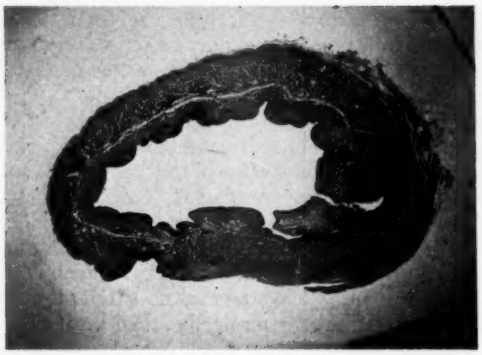

FIG. 5. Histologic section of specimen one hundred days after surgery, dog No. 559. Eighty per cent of the circumference of the tube contained all normal layers. Ten per cent of the circumference was composed of an inner layer of stratified squamous epithelium and an outer layer of fibrous tissue.

length in the relaxed state) were rotated, one from the proximal cut end of the esophagus and the other from the distal cut end of the esophagus. The ends of the two rotated flaps were sutured to each other to bridge the defect. Of these, four of the animals showed complete tubulation with good swallowing function but the fifth died on the nineteenth postoperative day as a result of breakdown of the anastomosis and retraction of the flaps.

COMMENTS

Previous experimental work [6,7] demonstrated that even a narrow open strip of esophageal and pharyngeal wall tubulated to form a functional swallowing tube proved to be more pliable and more distensible than tubes made from skin flaps or lined by split thickness skin. In these experiments large segments of the esophagus and pharynx were partially resected, leaving only a narrow strip of the esophageal wall in continuity with the intact pharynx above and the esophagus below. Despite the

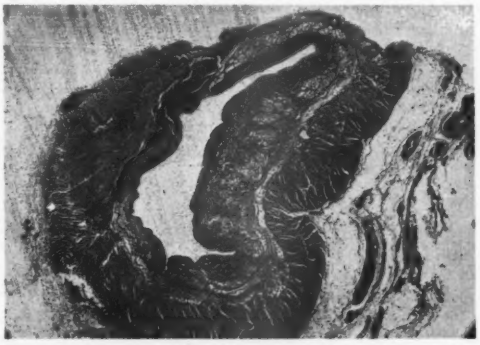

FIG. 6. Two hundred twenty-three days after operation, dog No. 564. The fibrous segment formed 5 per cent of the circumference of the tubulated area.

FIG. 7. Barium swallow in human subject after complete healing.

large surgical fistulas which were created, these intact strips underwent spontaneous tubulation resulting in functional swallowing organs.

The present experiments differed in that a segment of cervical esophagus was completely transected, leaving a defect 8 cm. in length (in the relaxed state) between the proximal and distal ends of the esophagus. Full thickness flaps were rotated from these cut ends to bridge the gap, producing a final anatomic situation which was similar to the earlier experiments. As in the previous experiments, no attempt was made to tubulate surgically this bridge of tissue. This decision was influenced by the spontaneous tubulation which occurred in the earlier experiments; also by the fear that the addition of too many sutures would impair the blood supply to the edges of the flaps, in turn resulting in narrowing of the viable segments. The final results demonstrated that open rotated flaps also will tubulate spontaneously.

The necessity of maintaining a strip of mucosal-muscular wall continuous with the esophagus below and the esophagus or pharynx above was clearly demonstrated. Breakdown of the suture line with complete retraction of the ends of the flaps resulted in fibrosis, complete obstruction and death from aspiration. The three animals in which there was partial separation of the suture line developed severe strictures which eventually caused the death of the animals.

The viability of the anastomosis was dependent on the blood supply to the tissue flap and successful tubulation was related to the length of the rotated flaps. The rotation of two short flaps, one from the distal cut end of the esophagus and one from the proximal cut end of the esophagus and pharynx, resulted in a higher percentage of successful results (80 per cent) as compared with a longer single flap rotated from the distal cut end of the esophagus (29 per cent).

The animals were allowed water relatively early. If the fistula was still present, some water escaped through the fistulous opening, but it was noted that the amount which came out of the fistula was considerably less than the amount taken. In instances where obstruction was present, the animal aspirated, coughed and refused further feedings.

Microscopic results indicated that a pseudopassage was created by a fibrous tissue reaction, probably to the salivary juices in the operative site. This fibrous cavity was quickly lined by outgrowth of epithelium from the longitudinal mucosal edges of the rotated flaps. With the passage of time, the fibrous wall of the new tube gradually contracted drawing the longitudinal edges of the original flaps closer and closer together. The final tube though grossly narrowed was soft, pliable and distensible. Normal layers (mucosa, muscularis mucosa and muscularis) formed 95 per cent of its wall.

To date, a similar operative procedure has been carried out in two human subjects. In both instances the flaps after rotation were sutured closed over a nasogastric tube (not left open as they were in the dogs). In both instances healing progressed without complications and both patients developed a functional swallowing apparatus. (Fig. 7.) This procedure, however, should be reserved for smaller defects. Clinically, it has been most helpful in reconstruction following resection of pyriform sinus lesions which secondarily involved the postcricoid area.

SUMMARY

Animal experiments demonstrated that full thickness flaps of esophagus and pharynx can be rotated to reconstruct surgical defects of the cervical esophagus. Because of the blood supply of the esophagus success can be expected only when the flaps are kept relatively short. The procedure has been carried out successfully in two human subjects.

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CASE REPORTS

Congenital Aneurysm of the Jejunum

HENRY HUG, M.D.* AND CHARLES D. BRANCH, M.D., *Peoria, Illinois*

From the Department of Surgery, St. Francis Hospital, Peoria, Illinois.

MASSIVE hemorrhage from the gastrointestinal tract is a frequent problem confronting the surgeon. The most common source is the stomach and duodenum. There are numerous etiologic causes found in the small intestine; however, the case to be reported is only the second that we can find in a survey of the literature. Rathmell, Horwell and Greeley [1] in their report reviewed the literature and while they found reports of twenty-three patients with rupture of an aneurysm of a gastric artery, no aneurysm was found in the jejunum. They described a patient with an aneurysm of the jejunum producing fatal intestinal hemorrhage.

CASE REPORT

This twenty-two year old white woman, gravida 1, para 0, was admitted to the hospital on the obstetric service with a pregnancy at term. She was delivered of a normal female infant. There was an uneventful postpartum course until forty-eight hours following the delivery at which time she had two bouts of bleeding from the rectum; the first one was tarry and the second one contained bright red blood. At the time she was examined it was found that no mass was palpable in the abdomen and there was no tenderness. Proctoscopic examination was then performed and outside of old blood in the rectum, nothing further was observed. Twenty-four hours later she suddenly went into shock and had numerous stools composed almost entirely of bright red blood. The blood pressure, which had been within normal limits, fell to 40/0 mm. Hg and over a period of three hours she received 4,000 ml. of blood without any significant rise in the blood pressure. Because of the continuous massive hemorrhage without hematemesis, and the only manifestation being pure blood passed by rectum, operation was advised. Exploratory laparotomy was carried out through a right rectus incision. On opening the abdomen it was found that from a point 40 cm. from the ligament of Treitz the jejunum, terminal ileum, and colon contained blood. There was no blood above this point. The stomach and jejunum were also normal to inspection and showed no evidence of distention. In the jejunum, approximately 40 cm. from the ligament of Treitz, a tumor was palpable. This was quite small and was on the mesenteric side. Obviously the bleeding was arising from this mass. A segment of jejunum measuring 10 cm. in length and containing the tumor was removed and an end to end anastomosis was performed. The patient's condition was good following surgery. The hemoglobin was 10.2 gm. and hematocrit 32 per cent. Following this the patient had an uneventful recovery and was discharged seven days after surgery.

On gross examination the specimen consisted of a portion of small bowel measuring 10 cm. in length. When opened, a small raised dark red nodularity was found in the mid-portion of the excised loop. This nodularity was 5 mm. in diameter, arising from the mesentery attachment and was largely submucosal. (Fig. 1.)

Microscopic examination revealed a healthy pattern of jejunal mucosa except for the presence of a dilated thick-walled arterial structure which had its base within the submucosal soft tissue resting upon the muscularis of the bowel wall. Serial sections disclosed that this was an aneurysmal development from a normal size medium artery arising in the submucosa. The wall of the aneurysm was scarred and attenuated. Intimal thickening was prominent and the elastic tissue stains showed loss of elastic fibers. There was a

* Present address: Children's Hospital, Buffalo, New York.

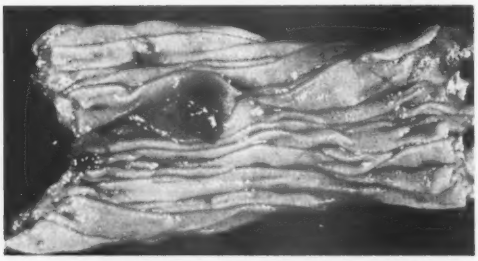

FIG. 1. Photograph of opened jejunum showing nodularity.

perforation or rupture of this aneurysm in the mid-portion of the mucosal aspect. (Fig. 2.)

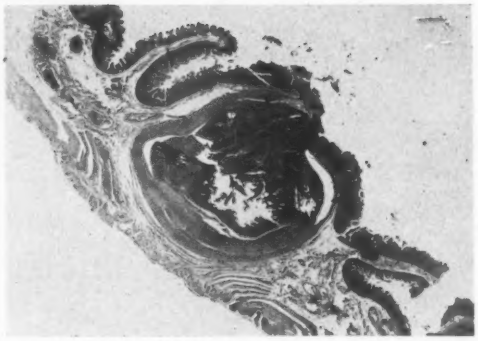

FIG. 2. Photomicrograph of nodularity showing aneurysmal development with perforation. Magnification × 10.

COMMENTS

The differential diagnosis of bleeding from the gastrointestinal tract has been discussed many times. The fact that this patient had had no vomiting of blood seemed to rule out the possibility of bleeding from the stomach or esophagus. There was no history of ulcer but, of course, one in the duodenum could not be ruled out because hematemesis is not always present. The other possibilities that could occur in the small bowel such as a polyp, fibroma and numerous other rare conditions were considered. However, with the patient in such critical condition, immediate operation was performed with large amounts of blood available for transfusion. Microscopic examination of the section proves this to be an artery. There was no evidence of arteriosclerosis, active inflammation, or positive result of a serologic test for syphilis. By the process of exclusion the lesion was considered to be congenital in origin.

SUMMARY

A second case of massive intestinal hemorrhage due to rupture of a congenital aneurysm of the jejunum is reported. This type of a case emphasizes the need for abdominal exploration in those cases in which the source of massive bleeding cannot be determined.

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Multiple Leiomyosarcomas of the Jejunum with Metastasis to Inguinal Lymph Nodes

T. K. Das Gupta, M.D., Leonard H. Kolb, M.D. and John G. Gruhn, M.D.,
Chicago, Illinois

From the Departments of Surgery and Pathology, Mount Sinai Hospital, and the Division of Oncology, The Chicago Medical School, Chicago, Illinois.

Leiomyosarcoma of the small intestine is uncommon in the experience of any single surgeon. Nevertheless, by 1955 Starr and Dockerty [1] surveyed 230 reported cases of myomatous tumors of the small intestine and added seventy-six cases of their own from the Mayo Clinic. In over 60 per cent of the latter cases, the lesion was malignant. In previous reviews, the emphasis has been on the frequency with which these tumors ulcerate and bleed, the extensive necrosis which they undergo and the incidence of malignancy [2].

The occurrence of metastasis to the lymph nodes is extremely rare. Starr and Dockerty reviewed four cases in which there were metastases in the lymph nodes but failed to find any illustrated histologic documentation. In view of this observation, they and others advised that surgical management of leiomyosarcoma consist of adequate resection of the lesion and the surrounding tissue without attempting to resect the regional nodes and related lymphatics. More recently, Darling and Welch [3], in a review of eight cases of leiomyosarcoma of the small bowel at Massachusetts General Hospital from 1913 to 1957, found only one patient in whom the lymph nodes were involved and this was by direct extension. Humphreys [4] recalled an unreported case of an inguinal metastasis from a gastric leiomyosarcoma which occurred fourteen years after the diagnosis was first established. The relative rarity of the disease itself, the infrequency of multiple primary sites and the lack of an illustrated report of metastasis to the lymph nodes warrants the following case report. To the best of our knowledge this is the first illustrated case of metastasis to the lymph nodes from a leiomyosarcoma in the jejunum. The case is also unusual in that the patient was admitted because of a mass in the right side of the groin which was thought to be a hernia or a lymph node enlargement of an undetermined type, but he did not have gastrointestinal symptoms. The mass was biopsied and found to be a metastatic leiomyosarcoma; subsequent radiographic examinations for a primary site revealed multiple sources within the jejunum.

CASE REPORT

A seventy-two year old white man was admitted to Mount Sinai Hospital on March 20, 1960, with a painless nontender inguinal mass on the right side which had been apparent and growing slowly in size for four months. There was no evidence of loss of weight. Physical examination of the right inguinal region revealed a mass 6 by 4 cm., oval in shape, over the fossa ovalis. In addition, the liver with a soft sharp edge was palpable two fingerbreadths below the costal margin. Neither spleno-

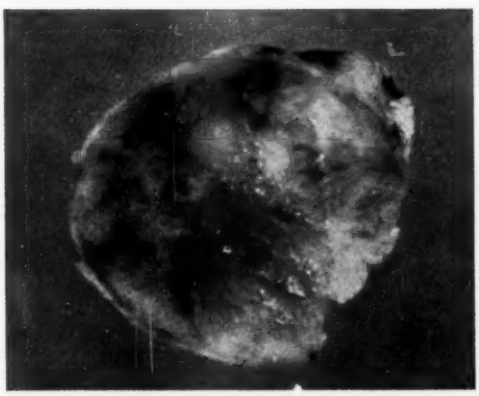
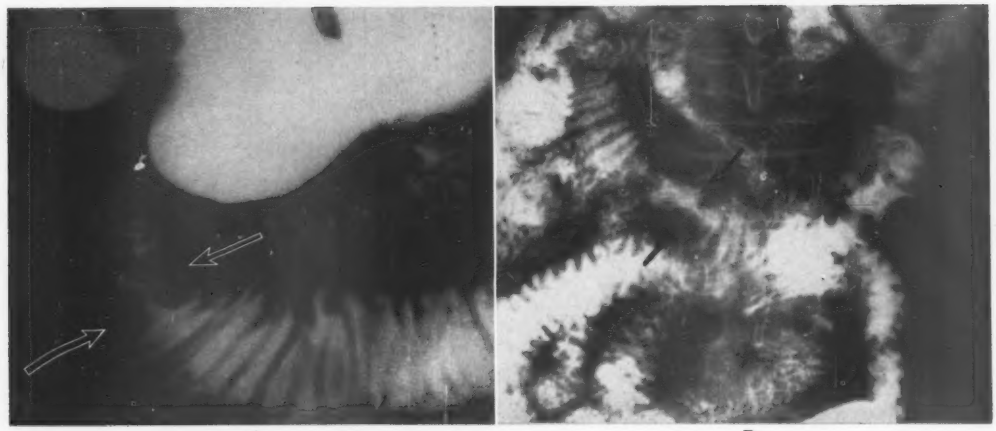


Fig. 1. Cut surface of a lymph node which has been replaced largely by fleshy tumorous tissue.



2A 2B

FIG. 2. Roentgenograms showing the filling defect in the proximal portion (A) and the distal portion (B) of the jejunum.

megaly nor any other detectable lymphadenopathy was present.

On admission, the laboratory studies disclosed the following: hemoglobin, 10.1 gm. per cent; hematocrit, 30.5 per cent; red blood cell count, 3.83 million per cu. mm.; white blood cell count, 8.650 per cu. mm.; and the differential blood count was within normal limits. The results of urinalysis, of analysis of the serum and of roentgenographic examination of the chest and the determinations of blood sugar and blood urea were noncontributory.

The inguinal mass was excised on March 22, 1960. The specimen consisted of two lymph nodes; one measured 5.5 by 3.5 by 2.5 cm., and the other was 3 by 2.5 by 2.5 cm. Externally the capsule was intact. Cut sections disclosed a bulging surface which appeared tan and fleshy. (Fig. 1.) Microscopic sections demonstrated a peripheral rim of lymphoid tissue but the bulk of the node was replaced by interlacing bundles of spindle-shaped cells with hyperchromatic moderately pleomorphic blunt end nuclei. Moderate numbers of mitotic figures were present in every field. Van Gieson's and Masson's stains disclosed little fibrous tissue. The Snook silver stain demonstrated a fine reticulin pattern between individual tumor cells. Phosphotungstic acid hematoxylin stain on Zenker-fixed tissue demonstrated myofibrils.

The pathologic diagnosis was metastatic leiomyosarcoma in the right inguinal lymph nodes.* The patient was readmitted as soon thereafter as feasible to establish the primary site. He had been essentially asymptomatic at home. A second physical examination disclosed no additional relevant findings save for the well healed scar in the right side of the groin.

Further laboratory studies included repeated determinations of hemoglobin; the results persistently approximated 10 gm. per cent indicating mild iron-deficiency anemia. The stool was positive for occult blood on three occasions during the time the patient was on a meat-free diet. The results of analyses for blood sugar, blood urea nitrogen, serum electrolytes, serum proteins, albumin and globulin, protein electrophoresis and of studies of liver function, bone marrow aspiration, serum carotene and serum enzymes were within normal limits.

Roentgenologic studies of the upper gastrointestinal tract revealed two areas of filling defect, one in the proximal portion of the jejunum and the other in the distal part of the jejunum. (Fig. 2A and B.) Repeated examinations indicated this filling defect was persistent. The results of lower gastrointestinal studies were negative.

After the primary sites of leiomyosarcomas were roentgenographically demonstrated in the jejunum, an exploratory operation was performed. One mass was found in the proximal portion of the jejunum about 1.5 inches from the ligament of Treitz and two similar masses were present in the distal part of the jejunum. No other gross site of disease was noted. The liver and spleen were normal, and the pre- and para-aortic lymph nodes were free of metastases on inspection and palpation. A wide segmental resection of the jejunum, including its mesentery, was performed. Intestinal continuity was established with an end to end anastomosis. Biopsy of the liver was also performed.

The patient's postoperative course was without complications and he was discharged twelve days

* Diagnostic consultation with Dr. Eleanor Humphreys, Billings Hospital, University of Chicago, is appreciatively acknowledged.

FIG. 3. Three foci of leiomyosarcoma in the jejunum. Large unopened segment includes two ellipsoidal tumor masses, small opened portion includes a third tumor mass.

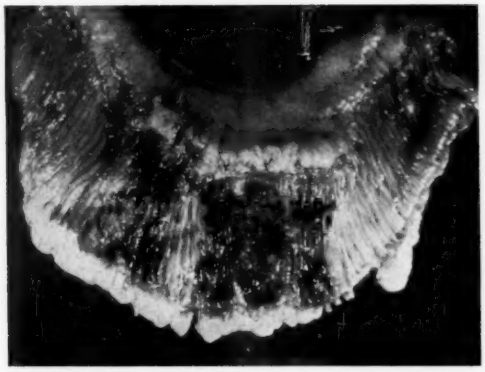


FIG. 4. Surface of predominantly intramural tumors in the jejunum is focally hemorrhagic and ulcerated.

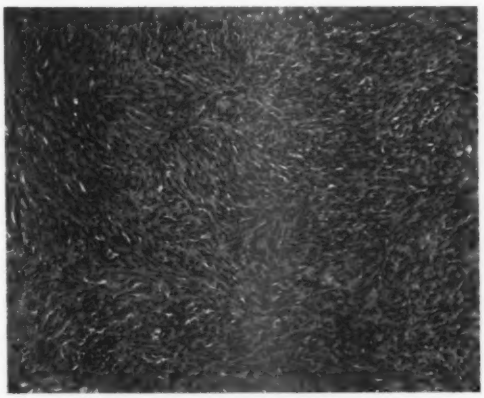


FIG. 5. Mid-power photomicrograph of leiomyosarcoma showing typical pattern from node. The same pattern was demonstrated in tumorous tissue taken from the jejunum. (Original magnification × 120.)

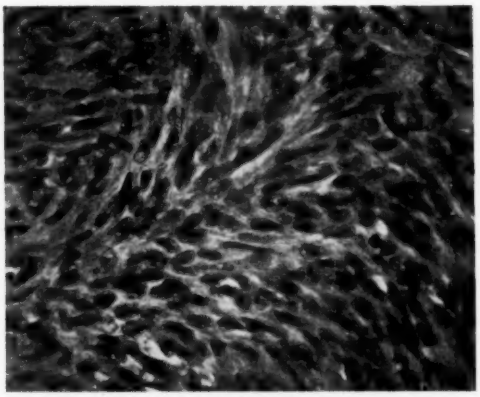


FIG. 6. High power photomicrograph leiomyosarcoma showing typical pattern in jejunum. The same pattern was demonstrated in tumorous tissue taken from nodes. (Original magnification × 480.)

later. The patient was on a regular diet at the time of discharge.

During pathologic examination of the specimen obtained during the operation (Figs. 3 and 4), the small finger of the examiner could barely be passed through the partially occluded lumen at the tumor sites. The cut section of the tumor demonstrated firm tan fleshy tissue predominantly intramural, extending from the luminal surface throughout the entire wall. The luminal surface above the tumor was ulcerated, hemorrhagic and focally covered with necrotic debris. The serosa was not penetrated by the tumor. The mesenteric lymph nodes were free of tumorous tissue. Histologic sections of the leiomyosarcoma of the jejunum were precisely similar to the metastases previously observed in the inguinal lymph nodes. (Figs. 5 and 6.) The biopsy of the liver disclosed normal hepatic tissue.

COMMENTS

In this case, several interesting features were demonstrated. Since the patient had a mass in the right side of the groin at the outset without gastrointestinal symptoms, the possibility of a tumor in the small bowel was not considered until after excision biopsy of the node.

The persistent results of tests for occult blood in the stool and the hemoglobin value of

10.1 gm. per cent directed our attention to a bleeding source in the gastrointestinal tract. Intestinal bleeding has been present in 53 per cent of symptomatic patients [5]. Moreover, pathologic examination of the specimen revealed an impending obstruction which occurs in 70 to 76 per cent of patients. Roentgenologic examination of the upper gastrointestinal tract has provided previously a correct preoperative diagnosis of a tumor in the small bowel in 84 per cent of the patients.

Multiplicity of intestinal sites of leiomyosarcoma is uncommon. Only two of the forty-one cases reported by Starr and Dockerty were multiple [1]. In the instance reported herein, the lesions appeared autochthonous rather than metastatic within the jejunum.

The rare occurrence of lymph node metastases from leiomyosarcoma of the small bowel should not be dismissed entirely when planning surgical excision of these tumors.

SUMMARY

A case of leiomyosarcomas of the jejunum of a patient with obvious lymph node metastases in the right side of the groin is reported. This is the first reported case of leiomyosarcomas of the jejunum metastasizing to inguinal lymph nodes.

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Papilloma of the Ampulla of Vater

MARION C. ANDERSON, M.D. AND WESLEY H. GREGOR, M.D., *Chicago, Illinois*

From The Department of Surgery, Northwestern University Medical School and Passavant Memorial Hospital, Chicago, Illinois.

PAPILLOMA of the ampulla of Vater is a rare benign lesion which is difficult to recognize before operation. A recent experience with this problem, the first to be demonstrated preoperatively, prompted this report which includes a compilation of all cases cited in the available world literature.

CASE REPORT

A forty-nine year old Caucasian man (A. H.), was admitted to Passavant Memorial Hospital on February 13, 1960, for treatment of an acute bronchitis associated with chronic pulmonary emphysema. Past history revealed chronic dyspepsia, particularly following the intake of fatty or fried meals, and periodic bouts of nonradiating pain in the upper right abdominal quadrant, which had subsided spontaneously. During the month before admission there had been a 15 pound weight loss.

Physical examination revealed a thin white man in moderate respiratory distress. The temperature was 98°F., pulse 104 and blood pressure 136/92 mm. Hg. The chest had an increased anteroposterior diameter and there were many expiratory rhonchi. The expiratory phase of respiration was prolonged. The abdomen was soft, but slightly tender in the upper right quadrant. There were no palpable organs or masses.

Laboratory studies including a complete hemogram and urinalysis were within normal limits. Chest roentgenograms revealed a patchy increase in density in the upper right and lower lung fields and emphysematous changes in both lungs. The sedimentation rate, serologic tests, blood urea nitrogen, fasting blood sugar, alkaline phosphatase, van den Bergh, bromsulphalein and electrolyte determinations were within normal limits. Pulmonary function studies revealed moderate obstructive emphysema with slight bronchospasm which was relieved by bronchodilators. Cholecystograms revealed less than average concentration of dye within the gallbladder but no evidence of stones. A barium meal demonstrated a smooth filling defect measuring 1.5 in diameter on the medial wall of the second portion of the duodenum. (Fig. 1.)

The patient responded well to treatment with erythromycin, 250 mg. four times a day, potassium iodide and Alevaire® and Isuprel® inhalations. Repeat chest roentgenograms were within normal limits on February 23, 1960. Operation for the duodenal lesion was recommended and performed on February 29, 1960.

FIG. 1. Roentgenogram demonstrating the lobular 1.5 cm. filling defect on the medial wall of the second portion of the duodenum.

TABLE 1

Source	Date	Age (yr.)	Sex	Clinical Findings	Gall-stones	Jaun-dice	Size	Histology	Radiology	Operation	Results	Comment
Archibald [8]	1930	60	F	Nausea	No	Yes	Tiny	Papilloma	None	Duodenotomy, local excision; cholecystectomy 3 mos. before	Living and well	...
Christopher [9]	1933	74	F	Abdominal pain; vomiting	Yes	No	5 mm.	Adenoma	None	(1) Cholecystotomy; (2) Catheter placed thru CBD into duodenum	Died	Fecal fistula developed; tumor found at autopsy
Landivar [10]	1934	49	M	Severe intermittent RUQ pain	No	Yes	Olive size	Papilloma	None	Duodenotomy; local excision	Living and well	...
Cabot case [11]	1936	55	F	RUQ pain; weight loss	Yes	Yes	1 cm.	Papilloma	Pressure defect on lesser curvature, stomach	Biliary tract operation; type unknown	Died	Autopsy 3 weeks postoperatively demonstrated biliary fistula; tumor
Grasmik [12]	1937	58	M	Anorexia; weight loss	No	Yes	2–2.5 cm.	Papilloma	None	Local excision; reimplantation of pancreatic and common bile ducts	Living and well	...
Mallet-Guy [13]	1939	56	F	Upper abdominal pain	Yes	Yes	Grain of corn	Benign polyp	Operative cholangiogram at 4th operation showed filling defect	Duodenotomy; local excision	Living and well	...
Horsely [14]	1941	60	M	Upper abdominal pain	No	Yes	1.5 by 1 cm.	Papilloma	None	Pancreaticoduodenectomy	Died	Death 5 days after operation
Grove, Rasmussen [15]	1944	59	M	Nausea; emesis; weight loss	No	Yes	Walnut	Papilloma	None	Duodenotomy; local excision	Recovered	Died 2 yrs. later of unrelated cancer
del Valle, Sanchez-Zinny [16]	1946	49	F	RUQ pain; diarrhea	No	Yes	Chick pea	Adenoma	Scout and pneumoperitoneum films negative except enlarged liver	Duodenotomy; local excision; ligation of Wirsung s duct; reimplantation of CBD; choledochostomy	Living and well	...
Baker, Caldwell [17]	1947	49	M	Fever; chills	No	Yes	Not recorded	Papilloma	Nonvisualizing gallbladder	Cholecystoduodenostomy; no excision; frozen section taken	Well 2 yrs. later	Tumor not removed
Basora-Deliffo, Lugo [18]	1949	2½ mos.	F	Vomiting, diarrhea, acholic stools	No	Yes	4–5	Adenofibroma	None	None	Died	Autopsy showed obstructive biliary disease
Cattell, Pyrtek [19]	1950	53	F	Epigastric pain; weight loss	No	Yes	4 mm.	Papilloma	None	Cholecystojejunostomy; local excision	Living and well	...
Cattell, Pyrtek [19]	1950	33	F	RUQ pain; weight loss	No	No	4 mm.	Papilloma	None	Previous cholecystectomy; choledochojejunostomy; local excision choledochostomy	Living and well	...
Wheelock et al. [20]	1950	64	M	Heavy sensation in RUQ; weight loss	No	Yes	5 mm.	Papilloma	Deformity of duodenal bulb	Duodenotomy; local excision	Living and well	...
Smith, Blakemore [21]	1951	54	F	RUQ pain; emesis; chills; fever	No	Yes	1 cm.	Adenomatous polyp	T tube cholangiogram after first operation showed filling defect at ampulla of Vater	(1) Cholecystectomy and choledochostomy; (2) duodenotomy; local excision	Living and well	Duodenotomy 2 mos. after lesion demonstrated on T tube cholangiogram
Giraid et al. [22]	1952	69	M	Fever	No	Yes	2 cm.	Adenoma	Preoperative cholecystogram visualized without stones; external pressure noted on duodenum	Choledochotomy; duodenotomy; choledochoduodenostomy; local excision	Living and well	...

TABLE 1 (*Continued*)

Source	Date	Age (yr.)	Sex	Clinical Findings	Gall-stones	Jaun-dice	Size	Histology	Radiology	Operation	Results	Comment
Kirsteins et al. [23]	1953	44	M	Emesis; nausea	No	Yes	2 cm.	Adenoma	None	Duodenotomy; local excision with reimplantation of pancreatic and common bile ducts; cholecystoduodenostomy	Living and well	...
Picard et al. [24]	1953	70	F	RUQ pain; fever	No	Yes	Cherry stone	Adenoma	Nonvisualization of gallbladder	Local excision; local reimplantation of common bile ducts; cystostomy and cholegastroenterostomy	Living and well	...
Van Weel [25]	1953	58	F	None	No	Yes	Small	Papilloma	None	Duodenotomy; local excision	Unknown	...
Van der Zwaag [26]	1956	54	M	RUQ pain; fever	No	Yes	Marble size	Papilloma	Preoperative cholangiogram showed dilated CBD; operative cholangiogram showed filling defect	Delivered tumor with bile duct spoon through choledochotomy	Living and well	Cholecystectomy for stones 3 yrs. before
Terrase et al. [27,28]	1958	58	M	Anorexia	Yes	Yes	Small	Papilloma	Deformity of duodenal bulb	Choledochotomy; cholecystogastrostomy; duodenotomy; local excision	Living and well	...
Terrase et al. [27,28]	1958	69	F	Epigastric pain	No	Yes	Small	Papilloma	None	Choledochotomy; duodenotomy; local excision	Living and well	...
Terrase et al. [27,28]	1958	66	F	Subcostal tenderness	No	Yes	Small	Papilloma	Preoperative cholangiogram showed large gallbladder without stones	Cholecystotomy; choledochotomy; duodenotomy; local excision	Living and well	...
Brombart et al. [29]	1958	63	M	RUQ pain; vomiting	No	No	Olive size	Adenoma	Faint visualization of gallbladder	Duodenotomy; local excision	Living and well	...
Brombart et al. [29]	1958	44	M	Epigastric pain; nausea; vomiting	Yes	Yes	Small	Papilloma	Cholangiogram showed stone at junction of hepatic ducts; operative cholangiogram showed defect at ampulla	Duodenotomy; local excision with electrocautery; cholecystectomy	Living and well	...
Brombart et. al. [29]	1958	64	F	RUQ pain	Yes	No	Pea size	Adenoma	Cholangiogram showed CBD stone	Duodenotomy; local excision	Living and well	Cholecystectomy 4 yrs. before
Brombart et al. [29]	1958	65	M	Substernal and left subcostal pain	Yes	No	Small	Adenoma	Cholecystogram showed stones; operative cholangiogram showed narrowing at distal CBD	Duodenotomy; local excision	Living and well	...
Lucrelli [30]	1959	63	?	RUQ pain	No	Yes	Not recorded	Papilloma	Operative cholangiogram showed defect at distal CBD	Choledochoduodenostomy; local excision	Living and well	...
Rock, Fisher [32]	1959	70	M	Anorexia; nausea; weight loss vomiting	No	Yes	5 mm.	Papilloma	Nonvisualization of gallbladder	Pancreaticoduodenectomy	Living and well	Cholecystojejunostomy 1 mo. before
Anderson, Gregor	1960	49	M	Fatty food intolerance; vomiting	No	No	2 cm.	Papilloma	Filling defect on medial wall of duodenum at level of ampulla of Vater	Duodenotomy; local excision; cholecystectomy	Living and well	...

NOTE: RUQ, right upper quadrant; CBD, common bile duct.

FIG. 2. Gross appearance of papilloma of ampulla of Vater prior to local excision.

The abdomen was entered through a midline upper abdominal incision. The result of exploration was negative except for a palpable mass on the medial wall of the second part of the duodenum. The duodenum was mobilized by incising the lateral peritoneal attachments, and the tumor was exposed through a 3 cm. duodenotomy incision. The ampullary area was replaced by a 1.5 by 2 cm. lobular adenomatous appearing lesion. (Fig. 2.) The common bile duct was of normal size and thickness. A soft rubber catheter introduced into the bile duct just below the cystic duct junction entered the duodenum directly through the tumor.

The adenomatous mass and a 1 cm. cuff of adjacent duodenal wall was excised. Frozen section studies revealed no evidence of malignancy. Both the bile and pancreatic ducts were transected as they entered the duodenum and each was sutured to the duodenal defect with 5 to 0 arterial silk. (Fig. 3.) A long-armed T tube was inserted into the common duct; a No. 18 gauge polyethylene catheter was introduced into the pancreatic duct and held in place with a single silk suture. Both of these tubes extended into the third portion of the duodenum. The T tube was brought through a stab wound lateral to the main incision. The duodenotomy was closed with two layers of interrupted sutures; a cholecystectomy was performed and the abdominal incision was closed after inserting two Penrose drains in the right lateral abdominal gutter.

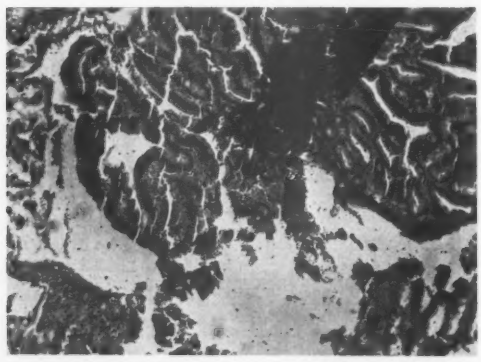

FIG. 4. Microscopic appearance of papilloma of ampulla of Vater. Original magnification × 100.

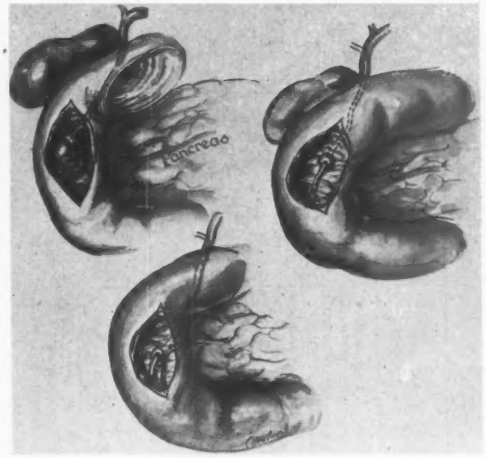

FIG. 3. Illustration of procedure of local excision of ampullary papilloma with reimplantation of both bile and pancreatic ducts into the duodenal defect.

The patient made an uneventful recovery and was discharged on March 11, 1960. During the subsequent year there has been no recurrence of discomfort, and he has gained over 40 pounds. Upper gastrointestinal roentgenograms six months following operation demonstrated a normal duodenum and no evidence of the small cannula in the pancreatic duct. The T tube was removed two months postoperatively.

Histologic studies revealed chronic inflammation of the ampulla of Vater, papilloma of the ampulla of Vater (Fig. 4), and chronic cholecystitis with no evidence of stones.

REVIEW OF THE LITERATURE

A total of thirty cases of benign epithelial tumor of the ampullary area were reviewed, including the present report. (Table 1.) Lesions

which histologically were not adenomatous or did not arise from the ampulla were not included. Hence, cases of ampullary melanoma [1], lymphangioma [2], carcinoid [3], and papilloma of the duodenal mucosa [4,5] have been excluded. Also, those cases previously reported as ampullary adenoma or papilloma, but not adequately proved because of insufficient information were excluded [6,7].

In twenty-six patients the diagnosis of a benign ampullary tumor was established by operation. In three patients the specimen was discovered at autopsy; however, two of these were overlooked at previous biliary tract operations. The average age at the time of diagnosis was 58.2 years, excluding one congenital tumor in an infant. The ratio of male to female subjects was 1:1. Symptoms usually suggested biliary tract dysfunction, and included abdominal pain, fatty food intolerance, anorexia, nausea and vomiting. Jaundice was present in twenty-four and absent in five. None of the previous lesions were clearly demonstrated preoperatively with roentgenograms, although in eleven patients the roentgenograms suggested biliary tract disease. The size of benign ampullary tumors varied from 4 mm. to that of a walnut; the average diameter was approximately 1 cm. Seven patients had associated biliary calculi.

Of twenty-eight operated patients, twenty-three were treated by local excision of the ampullary tumor. Bile and pancreatic ducts were usually reimplanted in a manner similar to that employed in the present report; although in one patient the pancreatic duct was ligated. More formidable choledochoduodenostomy or choledochojejunostomy was undertaken in several instances. Three patients also had biliary diversionary procedures in which a retained gallbladder was anastomosed to some segment of the upper intestinal tract. Cholecystoduodenostomy was employed in one instance to bypass the ampullary area without complete local excision of the ampullary lesion. In another, a long catheter was passed through the common duct into the duodenum without local excision of the tumor. One papilloma was removed with a scoop during a common duct exploration. Two patients underwent pancreaticoduodenectomy for this benign lesion. Three patients died postoperatively, one following pancreaticoduodenectomy and in two death resulted from procedures which failed to remove the ampullary tumor. No serious complications were reported following local excision and reimplantation of the bile and pancreatic ducts into the duodenum.

COMMENTS

Benign epithelial tumors of the ampulla of Vater often cause symptoms suggesting biliary disease; however, in none of the cases reviewed was the lesion demonstrated in roentgenograms taken preoperatively. The present case, which was clearly visualized with air-contrast barium meal roentgenograms of the duodenum, emphasizes the importance of careful roentgenographic studies of the upper intestinal tract in patients with suspected biliary tract disease. In view of the high incidence of jaundice in patients with neoplasms in the ampullary area, these studies should be particularly informative when evaluating extrahepatic biliary tract obstruction.

In the present review only those cases of ampullary papilloma which produced sufficient clinical findings to merit operative intervention have been included. In 1895 Calzavara [32] reported a single case of ampullary papilloma, which was described as pea-sized, and which presented as an incidental autopsy finding. Baggenstoss [33] reported on twenty-five benign ampullary lesions which were discovered in the course of autopsy examination, all of which measured between 2 to 5 mm. in diameter. He attributed the prevalence of such findings to the structural relationships in this area, and to chemical irritants present in the gastrointestinal tract which may cause inflammatory changes in the ampulla of Vater.

Cattell and Prytek [19] have considered the possibility that adenomas of the ampulla may be premalignant lesions. They reported four cases of carcinoma of the ampulla which appeared to originate in previously benign tumors. Two of these patients had long histories of biliary tract disease which may have originated from pre-existing benign neoplasms. All tumors arising from the ampullary area should be locally excised and subjected to immediate frozen section histologic study before a decision is reached regarding the extent of the definitive operative procedure; otherwise, the resection may be inadequate in some instances and in others an unnecessarily radical operation may be undertaken.

Careful inspection of the ampullary area of

the duodenum by palpation, or by direct visualization if necessary, should be an integral part of any procedure performed for extrahepatic biliary obstruction.

Once a diagnosis of benign epithelial ampullary tumor has been established, local excision with reimplantation of the bile and pancreatic ducts into the duodenal defect is the treatment of choice. In view of the anatomic variability of the terminal biliary and pancreatic duct systems, the type of reconstruction may differ from case to case. The use of intraluminal tubes in both the bile and pancreatic ducts, to support the area of anastomosis during healing, produced no adverse effects in the case reported. The use of the gallbladder for diversionary purposes is less appealing in view of the high incidence of pre-existing chronic cholecystitis associated with these ampullary lesions.

The question of the advisability of cholecystectomy following operations which destroy the ampullary sphincter mechanism has not been completely settled. Doubilet and Mulholland [*34*] advise cholecystectomy whenever the sphincter of Oddi is divided, because the normal function of the gallbladder is dependent upon an intact sphincter mechanism. More recently, evidence has been presented which demonstrates adequate function of the gallbladder following sphincterotomy [*35*]. In our patient, the gallbladder was removed because of an acalculous chronic cholecystitis.

SUMMARY

A case of benign papilloma of the ampulla of Vater is presented and twenty-nine cases collected from the available world literature are reviewed.

Ampullary papillomas often produce symptoms of biliary tract disease; however, none of the previously reported cases were demonstrated roentgenographically before operation. The lesion in the present report was clearly demonstrated with air-contrast roentgenograms of the duodenum.

The treatment of choice for benign tumors of the ampulla of Vater is local excision and reimplantation of the terminal bile and pancreatic ducts into the duodenal wall. Such lesions should be studied histologically at the time of excision to establish the type of tumor and the presence or absence of malignancy.

Despite the rare occurrence of such tumors, they serve to emphasize the importance of careful inspection of the terminal portion of the bile duct in all operations performed on the biliary tract.

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Surgery Court Cases

HOWARD NEWCOMB MORSE,* *Chicago, Illinois*

LIPPARD VS. JOHNSON

Supreme Court of North Carolina

215 N. C. 384, 1 S. E. 2d 889

The patient, on the advice of his physician, procured the chief surgeon in charge of the Hickory Memorial Hospital in Hickory, North Carolina, to perform circumcision. In performing the operation the surgeon used a local anesthetic (Novocain®). There were a number of injections. At the point of the first injection a knot arose which developed into a blister. Thereafter the blister burst and a process of decay set in, eating out a portion of the tissue. The section covering the blister became black and hard and could not be removed without treatment with vaseline and by excision.

After undergoing treatment for some time the patient went to a specialist in Charlotte, North Carolina. Healing occurred after several weeks' treatment by the specialist, but left the patient in such condition that at times he suffered therefrom.

The patient filed an action in the Superior Court of Catawba County, North Carolina, against the surgeon to obtain damages for the injuries alleged to have resulted from negligence. The court dismissed the case, and the patient appealed. The Supreme Court of North Carolina sustained the decision of the lower court. The Supreme Court held that as no expert testimony was offered by the patient, evidence of physical injury as the proximate result of negligence on the part of the surgeon was insufficient for the jury.

The Court stated: "The plaintiff relied on his testimony and the testimony of his wife. There was no expert testimony . . . . the plaintiff has failed to . . . show that he has suffered any physical injury as a proximate result of any careless or negligent conduct of the defendant."

GLOVER VS. BURKE

Court of Appeals of Tennessee

23 Tenn. App. 350, 133 S. W. 2d 611

The patient had a cyst or chalazion on the underside of the upper eyelid. She consulted surgeon No. 1 in Lebanon, Tennessee, who told her that he could remove the cyst by a slight operation, that it would not cause her pain or affect her sight, and would be cured within a short time. She employed him and he performed the operation, after sterilizing his instruments and his hands. He everted the eyelid, made an incision, scraped out the tissue with a curette, and put some hydrogen peroxide and a 5 per cent argyrol solution on it, dressed and bandaged it. He instructed her to go home, remain quiet and not to touch it or her eye, so that it would not become infected.

She returned to his office every day for treatment for almost two weeks. He had an engagement to attend a medical meeting in St. Louis, and made arrangements with another doctor in Lebanon to treat her in his absence. The first doctor told her that her eye was doing nicely and was not infected when he examined her last; however, three or four days before he left he noticed a white circular ring in the iris around the outer portion, which gradually grew cloudy and remained cloudy.

* Counsellor at Law of the Supreme Court of the United States of America.

On the day after he left for St. Louis, the patient called on the other doctor, who examined her eye and found the "entire eyeball completely inflamed." He refused to treat it, as he was not an eye specialist, and advised her to consult a specialist at once. The eye specialist (surgeon No. 2) at the Vanderbilt University Hospital in Nashville found her eyeball badly infected, and as it grew worse under treatment for a few days, it became necessary to remove the eyeball.

The patient filed an action in the Circuit Court of Wilson County, Tennessee, against surgeon No. 1 to obtain damages for malpractice on the ground that the surgeon negligently treated her eye and did not use ordinary skill and ability. A jury returned a verdict for the patient and the court entered judgment accordingly. Surgeon No. 1 appealed.

The Court of Appeals of Tennessee sustained the decision of the lower court. The Court of Appeals ruled that surgeon No. 1 had not showed ordinary skill and ability in treating the patient's eye after he operated on her eyelid.

The Court of Appeals stated: "The . . . doctor at Lebanon says that her 'entire eyeball was completely inflamed' when he saw it and he refused to treat her, and the specialist at Vanderbilt says practically the same thing. Both said they thought it had been in that condition several days. The defendant (surgeon No. 1) said he noticed a white ring about the iris several days before he turned her over to the other doctor, and it gradually became cloudy, and remained cloudy. He evidently did not know or was negligent in not observing the infection when he assured her that her eye was doing nicely. At least it was a question for the jury to say whether he used the ordinary skill and learning possessed and exercised by members of his profession in good standing under similar circumstances."

Our Surgical Heritage

D. P. HALL, M.D., *Surgical Department, University of Louisville, Louisville, Kentucky*

UNITED STATES OF AMERICA

JOSEPH PANCOAST

JOSEPH PANCOAST, he of the steady hand and the keen eye, was born near Burlington, New Jersey, on November 23, 1805, the son of John and Anne Pancoast. In 1828 he received an M.D. degree from the Medical Department of the University of Pennsylvania after which he began to practice medicine in Philadelphia.

The Philadelphia Association for Medical Instruction was formed in 1830 and shortly after its inception Joseph Pancoast became connected with the Institution. It had a short but virile life and became extinct after six years. In 1831 Joseph Pancoast became Professor of Anatomy in the Geneva Medical College.

In 1835 Pancoast was elected an attending physician to the Philadelphia Hospital and close thereon became Physician-in-Chief of the Children's Hospital of Philadelphia. In 1838 Dr. George McClellan retired as Professor

of Surgery at Jefferson Medical College and Pancoast was his successor. It was about this time in his career that he edited Wistar and Horners Anatomy which was a very popular textbook in its day.

Joseph Pancoast in 1841 relinquished the Chair of Surgery to become Professor of Anatomy in Jefferson Medical College. He became a member of the attending staff of the Pennsylvania Hospital and continued this membership for ten years.

It may be said that Joseph Pancoast in many ways deserves to be known as the father of the American plastic surgery as he devised so many operations and also instruments to implement the procedures. He devised an ingenious operation for empyema of the thorax in which he raised a semicircular flap of tissue over the ribs. For the first time in 1862 he carried out a radical surgical operation for the cure of tic douloureux in which he divided the trunks of the fifth pair of nerves as they emerged from their foramina, at the base of the skull. In 1860 he devised a tourniquet to be used on the abdomen for compression of the lower end of the aorta, thus lessing blood loss from amputations of the thigh or hip.

Pancoast's "Treatise on Operative Surgery" was published in 1844 and was an immediate success, this was probably one of his outstanding works as up to that time very few texts of operative surgery had been published.

Joseph Pancoast died March 7, 1882. He was brilliant, bold and steadfast. He had the eye of an eagle and could cut with geometric precision because of his perfect knowledge of anatomy.

EUROPE

GUSTAV SIMON

GUSTAV SIMON, he of the Simon position for the operation of nephrectomy, was born in Darmstadt, Germany, on May 30, 1824. He studied medicine at Heidelberg and later at the University of Giessen where he received his M.D. degree in 1848.

For a few years he served as a Military Surgeon in the German army with great distinction and at this time published many papers relating to military surgery. The years of 1851 and 1852 were spent in Paris where he witnessed Jobert do many successful operations for the cure of vesicovaginal fistula. He returned to Darmstadt in the early months of 1852 where in close association with his colleagues he opened a private hospital. It was here that he devoted much of his time to surgery of the genitourinary organs.

In 1861 he became Professor of Surgery at the University of Rostock and Surgeon-in-Chief of the University Hospital. In 1866 he was made Chief of the Moabit Military Hospital at Berlin and was Surgeon-General of the reserves during the Franco-Prussian War. Gustav Simon became Professor of Surgery at the University of Heidelberg in 1868 and it was here that much of his early work came to fruition.

He was the author of several books among them were in 1854 "The Treatment of Vesicovaginal Fistula," in 1857 "Excision of the Spleen," in 1868 "Plastic Surgery."

Simon in 1869 was the first surgeon in Europe to excise the kidney.

In 1878 von Bruns performed a nephrectomy with a fatal result and it seems that this was much publicized and the operation of nephrectomy did not become in general use until antisepsis.

Simon is best known for his Simon position for nephrectomy and for his "Treatise on Surgery of the Kidneys," the latter stands as a monument to this many sided man's surgical endeavors and it probably was a basis for later developments in genitourinary surgery.

Gustav Simon died August 27, 1876, "thus the hand that guided his scalpel in deliberation and authority was stilled."

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